Document Number 3

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DOCUMENT-IDENTIFIER: US 5866434 A
TITLE: Graphitic nanotubes in luminescence assays

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BSPR:
Thus, U.S. 89/04919 is directed to methods for the detection of an analyte of interest in a sample, which method includes the steps of (1) forming a composition comprising (a) a sample suspected of containing an analyte of interest, (b) an assay-performance-substance selected from the group consisting of (i) analyte of interest or analog of the analyte of interest, (ii) a binding partner of the analyte of interest or its said analog, and (iii) a reactive component capable of binding with (i) or (ii), wherein one of said substances is linked to a label compound having a chemical moiety capable of being induced to luminesce, and (c) a plurality of suspended particles capable of specifically binding with the analyte and/or a substance defined in (b)(i), (ii), or (iii); (2) incubating the composition to form a complex which includes a particle and said label compound; (3) inducing the label compound to luminesce; and (4) measuring the luminescence emitted by the composition to detect the presence of the analyte of interest in the sample. Those same methods may be used to quantify the amount of analyte in a sample by comparing the luminescence of the assay composition to the luminescence of a composition containing a known amount of analyte.

BSPR:
Analogs of the analyte of interest, which may be natural or synthetic, are compounds which have binding properties comparable to the analyte, but include compounds of higher or lower binding capability as well. Binding partners suitable for use in the present invention are well-known. Examples are antibodies, enzymes, nucleic acids, lectins, cofactors and receptors. The reactive components capable of binding with the analyte or its analog and/or with a binding partner thereof may be a second antibody or a protein such as Protein A or Protein G or may be avidin or biotin or another component known in the art to enter into binding reactions.

BSPR:
Advantageously, the luminescence arises from electrochemiluminescence (ECL) induced by exposing the label compound, whether bound or unbound to specific binding partners, to a voltammetric working electrode. The ECL reactive mixture is controllably triggered to emit light by a voltage impressed on the working electrode at a particular time and in a particular manner to generate light. Although the emission of visible light is an advantageous feature the composition or system may emit other types of electromagnetic radiation, such as infrared or ultraviolet light, X-rays, microwaves, etc. Use of the

terms "electrochemiluminescence," "electrochemiluminescent" "electrochemiluminescence" "luminescence," "luminescent," and "luminesce" includes the emission of light and other forms of electromagnetic radiation.

BSPR:
The term "ECL moiety," "metal-containing ECL moiety" "label," "label compound," and "label substance," are used interchangeably. It is within the scope of the invention for the species termed "ECL moiety," "metal-containing ECL moiety," "organo-metallic," "metal chelate," "transition metal chelate" "rare earth metal chelate," "label compound," "label substance" and "label" to be linked to molecules such as an analyte or an analog thereof, a binding partner of the analyte or an analog thereof, and further binding partners of such aforementioned binding partner, or a reactive component capable of binding with the analyte, an analog thereof or a binding partner as mentioned above. The above-mentioned species can also be linked to a combination of one or more binding partners and/or one or more reactive components. Additionally, the aforementioned species can also be linked to an analyte or its analog bound to a binding partner, a reactive component, or a combination of one or more binding partners and/or one or more reactive components. It is also within the scope of the invention for a plurality of the aforementioned species to be bound directly, or through other molecules as discussed above, to an analyte or its analog. For purposes of brevity, these ligands are referred to as an assay-performance-substance.

DEPR:
Typical analytes of interest are a whole cell or surface antigen, subcellular particle, virus, prion, viroid, antibody, antigen, hapten, fatty acid, nucleic acid, protein, lipoprotein, polysaccharide, lipopolysaccharide, glycoprotein, peptide, polypeptide, cellular metabolite, hormone, pharmacological agent, synthetic organic molecule, organometallic molecule, tranquilizer, barbiturate, alkaloid, steroid, vitamin, amino acid, sugar, lectin, recombinant or derived protein, biotin, avidin, streptavidin, or inorganic molecule present in the sample. Typically, the analyte of interest is present at a concentration of 10.sup.-3 molar or less, for example, as low as 10.sup.-12 molar or lower.

DEPR:
The assay-performance-substance which is combined with the sample containing the analyte of interest contains at least one substance selected from the group consisting of (i) added analyte of interest or its analog, as defined above, (ii) a binding partner of the analyte of interest or its said analog, and (iii) a reactive component, as defined above, capable of binding with (i) or (ii), wherein one of said substances is linked to a compound or moiety, e.g. an ECL moiety capable of being induced to luminesce. The labeled substance may be a whole cell or surface antigen, a subcellular particle, virus, prion, viroid, antibody, antigen, hapten, lipid, fatty acid, nucleic acid, polysaccharide, protein, lipoprotein, lipopolysaccharide, glycoprotein, peptide, polypeptide, cellular metabolite, hormone, pharmacological agent, tranquilizer, barbiturate, alkaloid, steroid, vitamin, amino acid, sugar, nonbiological polymer (preferably soluble), lectin, recombinant or derived protein, synthetic organic molecule, organometallic molecule, inorganic molecule, biotin, avidin or streptavidin. In one embodiment, the reagent is an electrochemiluminescent moiety conjugated to an antibody, antigen, nucleic acid, hapten, small nucleotide sequence, oligomer, ligand, enzyme, or biotin, avidin, streptavidin, Protein A, Protein G, or complexes thereof, or other secondary binding partner capable of binding to a primary binding partner through protein interactions.

DEPR:
Analogs of the analyte of interest, which can be natural or synthetic, are typically compounds which have binding properties

comparable to the analyte, but can also be compounds of higher or lower binding capability. The reactive components capable of binding with the analyte or its analog, and/or with a binding partner thereof, and through which the ECL moiety can be linked to the analyte, is suitably a second antibody or a protein such as Protein A or Protein G, or avidin or biotin or another component known in the art to enter into binding reactions.

DEPR:
The invention is also directed to reagent compositions. Broadly, the reagent compositions may be any one of the components of the assay systems of the invention, i.e., (a) electrolyte, (b) label compound containing an ECL moiety, (c) functionalized fibrils to which an assay-performance-substance is bound, optionally bound to particles, including magnetically responsive particles, (d) analyte of interest or an analog of the analyte of interest, (e) a binding partner of the analyte of interest or of its analog, (f) a reactive component capable of reacting with (d) or (e), (g) a reductant, or (h) an electrochemiluminescence-reaction enhancer. The reagents may be combined with one another for convenience of use, i.e., two component, three component, and higher multiple component mixtures may be prepared, provided that the components are not reactive with one another during storage so as to impair their function in the intended assay. Desirably, the reagents are two-component or multicomponent mixtures which contain particles as well as one or more other components.

DEPR:
This example shows the synthesis of an enzyme detection reagent in ECL Analyzer. Ruthenium peptide fibrils synthesis: Tetrapeptide of FmocNH-Gly-Lys(N.sup..epsilon. -CBZ)-Phe-Gly-COOH was synthesized by conventional solution phase methods and this peptide (71 mg, 0.093 mmol) was reacted with a primary amine derivatized version of Ru(bpy).sub.3.sup.2+ (IGEN, Inc., Gaithersburg, Md.) (73 mg, 0.078 mmol), EDC (17.8 mg, 0.093 mmol) was used as a activating reagent, and HOBT (12.58 mg, 0.093 mmol) as a catalyst. The product FmocNH-Gly-Lys(NE-CBZ)-Phe-Gly-CO-NH-Tag (170 mg, 0.223 mmol) was deprotected with piperidine (96 ml) and methylene chloride (1.1 ml). The structure of the tetrapeptide-Ru(bpy).sub.3.sup.2+ compound was confirmed by 1H-NMR. To the solution of tetrapeptide-Ru(bpy).sub.3.sup.2+ (5 mg, 0.003 mmol) in methylene chloride (2 ml) was added carboxyl fibrils (54 mg). Then EDC (5.8 mg, 0.03 mmol) and HOBT (4 mg, 0.03 mmol) were added. The reaction mixture was stirred overnight. The fibrils were extensively washed with water, methanol, acetonitrile and methylene chloride. The product fibrils were treated with trimethylsilyl iodide (TMSI, 1 ml) in acetonitrile (4 ml) for 3 hours at 40.degree. C. The final product fibrils were extensively washed with water, methanol, acetonitrile, IGEN standard ECL assay buffer (IGEN, Inc., Gaithersburg, Md.) and methylene chloride.

DEPR:
To 2.97 ml suspensions of RPF (Fibrils-Gly-LysPhe-Gly-Ru(bpy).sub.3.sup.2+) (2.2 mg/mL) in standard ECL Assay Buffer (IGEN, Inc., Gaithersburg, Md.) was added either 30 .mu.L of 58.9 .mu.M trypsin (final concentration=0.59 .mu.M) in 1 mM HCl or 30 .mu.l of 1 mM HCl. The two suspensions were then rotated at room temperature. Periodically, the rotation was stopped, the suspension was quickly centrifuged, and the ECL of the aqueous supernatant was measured. The ECL results after 30 minutes of incubation showed that the ECL ratios of the samples (ECL with trypsin/ECL without trypsin) was 1.29. After 44 hours, the ECL ratio was 2.05. These results demonstrated that trypsin could be detected by its ability to hydrolytically liberate an electrochemiluminescent ruthenium label from fibrils.

DEPR:
To 2.97 ml suspensions of RPF (Fibrils-Gly-LysPhe-Gly-Ru(bpy).sub.3.sup.2+) (0.15 mg/mL) in

standard ECL Assay Buffer (IGEN, Inc., Gaithersburg, Md.) was added either 30 .mu.l of 34.2 .mu.M chymotrypsin (final concentration=0.34 .mu.M) in 1 mM HCl or 30 .mu.l of 1 mM HCl. The suspensions were rotated at room temperature. Periodically, the rotation was stopped, the suspension was quickly centrifuged, and the ECL of the aqueous supernatant was measured. The ECL results showed that initially (time=0) the ECL ratio of the samples (ECL with chymotrypsin/ECL without chymotrypsin) was 1.06. After 30 minutes of incubation, the ratio rose to 1.25, and after 23 hours of incubation, the ratio rose to 1.85. These data show that chymotrypsin activity could be detected by the ability of the enzyme to liberate an electrochemiluminescent label, Ru(bpy).sub.3.sup.2+, from a fibril solid support.

DEPR:
0.5 mg of NHS-ester fibrils were washed with 5 mM sodium phosphate buffer (pH=7.1) and the supernatant was discarded. 200 .mu.l streptavidin solution (1.5 mg in the same buffer) was added to the fibrils and the mixture was rotated at room temperature for 5.5 hours. The fibrils were then washed with 1 ml of the following buffers in sequence: 5 mM sodium phosphate (pH=7.1), PBS (0.1M sodium phosphate, 0.15M NaCl, pH=7.4), ORIGEN assay buffer (IGEN, Inc., Gaithersburg, Md.) and PBS. The streptavidin fibrils were stored in PBS buffer for further use.

DEPR:
The DNA probe assay is depicted in FIG. 4. The experiment was started with washing 115 .mu.g of BSA blocked avidin-fibrils and streptavidin fibrils (from Example 5) twice with 5 mM sodium phosphate buffer (pH=7.1). Each fibril was aliquoted into two tubes with .about.57 .mu.g in 100 .mu.l of the same buffer. One tube of (strept)avidin fibrils was mixed with 4 .mu.l of 4 nM biotinylated DNA (70 nucleotides) that was bound to a ruthenium tag labeled oligomer. The other tube was added with 4 .mu.l of ruthenium tag labeled oligomer (same concentration as in the biotinylated DNA sample) only for a control assay. The reaction mixtures were incubated at room temperature for 15 minutes and washed seven times with 300 .mu.l of ORIGEN assay buffer (IGEN, Inc., Gaithersburg, Md.). The fibrils were then suspended in 600 .mu.l ORIGEN assay buffer and aliquoted to two tubes for duplicate ECL counting, using gravity capture of the fibrils. The result of the ECL assay were summarized as follows:

DEPR:
To a suspension of bifunctional fibril (113 mg) in methylene chloride (8 ml) were added 4-dimethylaminopyridine (DMAP, 19.5 mg, 0.16 mmol) and 1,3 dicyclohexylcarbodiimide (DCC, 33 mg, 0.16 mmol) (FIG. 6). The mixture was stirred for 5 minutes, then 4-methyl-4'-(8-hydroxyoctyl) 2,2'-bipyridine (47 mg, 0.16 mmol) was added. The reaction mixture was stirred overnight at room temperature. The resulting product fibrils were extensively washed sequentially with DMF, 50% dioxane in water, methanol, and water. The fibrils were suspended in a mixture of ethanol (4 ml) and water (4 ml) and cis-dichlorobis (2,2'-bipyridine) ruthenium (II) dihydrate (45.2 mg, 0.087 mmol) was added. The mixture was refluxed for 5.5 hours at 110.degree. C. The ruthenium complex-modified fibrils were extensively washed with water, standard ECL assay buffer (IGEN, Inc., Gaithersburg, Md.), toluene, 50% dioxane in water, then sequentially refluxed in acetonitrile, ethylene glycol and methanol. The ruthenium complex-modified fibrils were reacted with TMSI (4 ml) in acetonitrile (4 ml) for 4 hours at 40.degree. C. to deprotect the CBZ group, then washed with methanol, water, and sodium hydroxide (1N). The final produce was dried under vacuum. The fibrils were then suspended in methylene chloride (5 ml) and triethylamine (5 drops) was added. To the suspension was added succinic anhydride (40 mg). The reaction mixture was stirred overnight at room temperature and the product was washed with methylene chloride, methanol, and water, then dried under vacuum. The carboxylic acid/ruthenium complex-modified fibrils were resuspended in dioxane (5 ml), then N-hydroxysuccinimide (100 mg) and EDC (167 mg) were added. The reaction mixture was stirred for 4 hours at room temperature. The

resulting NHS ester/ruthenium complex-modified fibrils were washed with dioxane and methanol. The NHS ester/ruthenium complex-modified fibrils were resuspended in dioxane (2 ml) and a solution of NAD analog in sodium bicarbonate (75 ml in 2 ml of 0.2M pH 8.6 NaHCO.sub.3) was added. The reaction mixture was stirred overnight at room temperature. The fibrils were then extensively washed with water, sodium bicarbonate (0.2M), and methanol, then dried under the vacuum to obtain the biosensor fibrils.

DEPR:
An enzyme biosensor was prepared containing a dehydrogenase enzyme to which has been conjugated both an analog of a nicotinamide adenine dinucleotide (NAD.sup.+) enzyme cofactor and an analog of ruthenium (II) trisbipyridine (Ru(bpy).sub.3.sup.2+). The NAD.sup.+ analog is tethered so that it can bind in the enzyme's cofactor binding site and behave naturally when bound (i.e., it can be reduced by the enzyme by the normal chemical mechanism in the presence of the natural substrate of the enzyme). Moreover, the Ru(bpy).sub.3.sup.2+ analog is tethered so that it can come into physical contact with the NAD.sup.+ (FIG. 10). In an ECL instrument such as an IGEN Origen.RTM. Analyzer (IGEN, Inc., Gaithersburg, Md.), NAD.sup.+ and its reduced form, NADH, promote Ru(bpy).sub.3.sup.2+ electrochemiluminescence to different extents. Thus, based on the light output, it can be determined whether NAD.sup.+, NADH, or some mixture of the two is present in a solution (F. Jameison et al., Analytical Chemistry, in press). Thus, the biosensor uses the differences between the efficiencies of the ECL reactions of Ru(bpy).sub.3.sup.+ to detect the extent of reduction of NAD.sup.+ and hence the presence of the enzyme's substrate. As an example, alcohol dehydrogenase catalyzes the reaction shown below; ethanol (reduced)+NAD.sup.+ (oxidized).fwdarw. acetaldehyde (oxidized)+NADH (reduced). An alcohol dehydrogenase-based ECL biosensor can convert ethanol to acetaldehyde, concomitantly converting NAD.sup.+ to NADH. Because the ECL properties of Ru(bpy).sub.3.sup.2+ immobilized on the biosensor depend on whether NAD.sup.+ or NADH is immobilized, the ECL of the enzyme biosensor can report the presence of ethanol. An attractive feature of the biosensor is that because during the ECL reaction the NADH form of the cofactor is re-oxidized to the NAD.sup.+ form, one biosensor molecule can be used repeatedly to detect multiple molecules of analyte.

DEPR:
ECL sensing of ethanol was carried out by mixing the ADH biosensor adsorbed beads (0.50-1.25 mg) or fibrils (0.04-0.10 mg) with a solution containing 0.1M sodium phosphate buffer (pH 7.2), 12 mM semicarbizide. Some samples also contained 0.5 mM of the analyte, ethanol. The solid supports coated with the biosensor were drawn into an IGEN Origen.RTM. ECL Analyzer (IGEN, Inc., Gaithersburg, Md.) and ECL was measured. Results of one such experiment are shown in FIG. 12. With both beads and fibrils, the ECL signal of the enzyme biosensor decreased in the presence of ethanol. This result is consistent with results obtained in solution studies (using non-immobilized NAD.sup.+ /NADH and non-immobilized Ru(bpy).sub.3.sup.2+) of the effect of the oxidation/reduction state of this NAD.sup.+ analog on Ru(bpy).sub.3.sup.2+ electrochemiluminescence. These results showed that fibrils can be used as a support for enzymes in ECL and in particular as a support for enzyme-based ECL biosensors. It should also be noted that the results seen with fibrils were similar to those seen with Dynal beads even though 20 times less fibrils was used.

DEPR:
Stock dispersions of chlorate oxidized fibrils, fibrils modified with PEG using benzoyl perioxide and fibrils modified with PEG by NHS ester coupling were prepared at 1.0 mg/ml in 50 mM potassium phosphate buffer, pH 7.0 with sonication. 2 mls of 10-fold serial dilutions of each were placed in each of 5 polypropylene tubes. 50 .mu.l of a stock solution of Ru(Bpy).sub.3 (approx. 10 .mu.M) in the same buffer was added to each tube and to 3 buffer blanks. Three

bufffer tubes without Ru(Bpy).sub.3 were also prepared. All tubes were mixed on a vortex mixer and allowed to incubate overnight. All tubes were centrifuged to separate the fibrils and 0.1 ml aliquots of the supernatant were transfered to new tubes and diluted with 1.0 mls of Origen.RTM. Assay Buffer (IGEN, Inc., Gaithersburg, Md.) and analyzed for Ru(Bpy).sub.3 by ECL using a Magnalyzers (IGEN, Inc., Gaithersburg, Md.). The level of Ru(Bpy).sub.3 remaining in the supernatant was an indirect measure of the amount that had been non-specifically bound to the fibrils (FIG. 13). For both of the PEG modified fibril materials substantially all of the Ru(Bpy).sub.3 remained in the supernatant at fibril levels up to 0.1 mg/ml. There was 20-30% decrease in the Ru(Bpy).sub.3 in the supernatant at 1.0 mgs/ml of these fibrils. In contrast, for the chlorate oxidized fibrils, there was almost no Ru(Bpy).sub.3 remaining in the supernatant at 1.0 mgs/ml and 20-30% decrease in the Ru(Bpy).sub.3 in the supernatant at 0.1 mg/ml of these fibrils without the PEG modification.

DEPV:
(ii) a binding partner of said analyte or a binding partner of said analogue; and

DEPV:
A is selected from ##STR7## --CR'.sub.2 --OY, N.dbd.Y or C.dbd.Y, Y is an appropriate functional group of a protein, a peptide, an enzyme, an antibody, a nucleotide, an oligonucleotide, an antigen, or an enzyme substrate, enzyme inhibitor or the transition state analog of an enzyme substrate or is selected from R'--OH, R'--NH.sub.2, R'SH, R'CHO, R'CN, R'X, R'SiR'.sub.3, ##STR8## and w is an integer greater than one and less than 200.

DEPV:
(d) a binding partner of the analyte of interest or of its analog;

CLPV:
(ii) a binding partner of said analyte or a binding partner of said analogue; and

CLPV:
(d) a binding partner of the analyte of interest or of its analog;

CLPW:
(ii) a binding partner of said analyte or a binding partner of an analogue of said analyte; and

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Document Number 4

Entry 4 of 9 File: USPT Dec 8, 1998

DOCUMENT-IDENTIFIER: US 5846485 A
TITLE: Electrochemiluminescent reaction utilizing amine-derived reductant

ASNM:
IGEN International Inc.

ASZZ:
IGEN International Inc.

PCPR:
This application is a division of application Ser. No. 08/196,315 filed Apr. 15, 1994 which is a continuation of application Ser. No. 07/266,914 filed Nov. 3, 1988, which is a continuation-in-part of application Ser. No. 06/858,354 filed Apr. 30, 1986 and a continuation-in-part of PCT U.S. application Ser. No. 87/00987 filed Apr. 30, 1987, and a continuation-in-part of application Ser. No. 07/369,560, filed Dec. 18, 1987 and a continuation-in-part of application Ser. No. 07/117,017, filed Nov. 4, 1987. Application Ser. No. 07/369,560, filed Dec. 18, 1987 is the national phase of PCT U.S. application Ser. No. 87/00987, filed Apr. 30, 1987, which is a continuation-in-part of application Ser. No. 06/858,354, filed Apr. 30, 1986. Additionally, U.S. application Ser. No. 188,258 filed Apr. 29, 1988, U.S. application Ser. No. 789,113 filed Oct. 24, 1985, and U.S. application Ser. No. 266,882 entitled "Microparticulate-Based Nonseparation Binding Assay", naming Shah, Hall, Powell and Massey, filed on even date herewith (CMS Docket No. 370068-2390), are all incorporated by reference herein.

BSPR:
Early ECL reactions involved the annihilation of oppositely charged radical ions, produced by sequential oxidation and reduction at an electrode using a double potential step, for example, as described in Faulkner, L. R., et al., Electroanalytical Chemistry, A. J. Bard (Ed.), Vol. 10, Marcel Dekker, N. Y., 1977, Ch. 1; Tokel-Takvoryan, N. E., et al., Chem. Phys. Lett., 1974, 25, 235; Velasco, J. C., et al., Inorg. Chem. 1983, 22, 822; Luong, J. C., et al., J. Am. Chem. Soc. 1978, 100, 5790; Abruna, H. D., J. Electrochem. Soc. 1985, 132, 842; and Abruna, H. D., J. Electroanal. Chem. 1984, 175, 321. Upon homogeneous electron transfer between the sufficiently energetic and oppositely charged radicals, an excited state of one of the precursors can be formed, and subsequent emission by the species in the excited state occurs. Additionally, so-called energy deficient mechanisms involving triplet-triplet annihilations have been reported. See Freed, D. et al., J. Am. Chem. Soc. 1971, 93, 2097; Wallace, W. L. et al., J. Electrochem. Soc. 1978, 125, 1430.

BSPR:
The "ECL moiety" or "metal-containing ECL moiety" is sometimes referred to as a "label", "label compound", "label substance", etc. It is within the scope of the invention for the species termed "ECL moiety", "metal-containing ECL moiety", "organometallic", "metal

chelate", "transition metal chelate" and "rare earth metal chelate"--when utilized in certain of the composition, reagent, kit, method, or system embodiments in accordance with the invention--to be linked to other molecules such as an analyte or an analog thereof, a binding partner of the analyte or an analog thereof, a further binding partner of such aforementioned binding partner, or a reactive component capable of binding with the analyte, an analog thereof or a binding partner as mentioned above. The above-mentioned species can also be linked to a combination of one or more binding partners and/or one or more reactive components. Additionally, the aforementioned species can also be linked to an analyte or its analog bound to a binding partner, a reactive component, or a combination of one or more binding partners and/or one or more reactive components. It is also within the scope of the invention for a plurality of the aforementioned species to be bound directly, or through other molecules as discussed above, to an analyte or its analog.

BSPW:
(ii) a binding partner of the analyte of interest or its said analog, and

BSPX:
(ii) a binding partner of the analyte of interest or its said analog, and

DEPR:
In addition to the metal-containing ECL moieties and the amines and amine moieties themselves, typical analytes of interest are a whole cell or surface antigen, subcellular particle, virus, prion, viroid, antibody, antigen, hapten, fatty acid, nucleic acid, protein, lipoprotein, polysaccharide, lipopolysaccharide, glycoprotein, peptide, polypeptide, cellular metabolite, hormone, pharmacological agent, nonbiological polymer (preferably soluble), synthetic organic molecule, organometallic molecule, tranquilizer, barbituate, alkaloid, steroid, vitamin, amino acid, sugar, lectin, recombinant or derived protein, biotin, avidin, streptavidin, or inorganic molecule present in the sample. In one embodiment, the reagent is an ECL moiety conjugated to an antibody, antigen, nucleic acid, hapten, small nucleotide sequence, oligomer, ligand, enzyme, or biotin, avidin, streptavidin, Protein A, Protein G, or complexes thereof, or other secondary binding partner capable of binding to a primary binding partner through protein interactions.

DEPR:
Typically, in assaying operations the metal-containing ECL moiety is linked directly or through one or more other molecules to the analyte of interest or an analog thereof. Analogs of the analyte of interest, which can be natural or synthetic, are typically compounds which have binding properties comparable to the analyte, but can also be compounds of higher or lower binding capability. When the metal-containing ECL moiety is linked to the analyte or said analog, through one or more other molecules, they are suitably a combination of one or more binding partners and/or one or more reactive components. Binding partners suitable for use in the present invention are well-known. Examples are antibodies, enzymes, nucleic acids, cofactors and receptors. The reactive components capable of binding with the analyte or its analog, and/or with a binding partner, are suitably a second antibody or a protein such as Protein A or Protein G, or avidin or biotin or another component known in the art to enter into binding reactions.

DEPR:
As described in commonly assigned U.S. application Ser. No. 266,882, entitled "Electrochemiluminescent Assays", naming Shah, Hall, Powell and Massey as inventors (CMS Docket No. 370068-2390), and filed on even date herewith, it is desirable, in performing assays disclosed herein, to incorporate particles in the assay composition or system. Binding of such a component, which in turn can be linked to an ECL moiety, to the particles greatly modulates the intensity of the ECL

signal generated by the ECL moiety, thereby providing a means of monitoring the specific binding reaction of the assay composition or system. Further information on this topic is set forth in the above-mentioned application, the subject matter of which is incorporated herein by reference.

DEPR:
The invention can also be employed in binding assays used in a competition format, where the ECL moiety is linked directly or through one or more other molecules to added analyte of interest. The binding partner is capable of specifically binding with the analyte of interest or the added analyte of interest which is linked to the ECL moiety. The analyte of interest and the added analyte of interest are suitably an antigen.

DEPR:
Alternatively, the binding partner is a primary binding partner of the analyte of interest. The assay sample contains the ECL moiety linked directly or through one or more other molecules to added analyte of interest. The binding partner is bound to suitable particles in the sample, and the particles are therefore capable of specifically binding with the analyte of interest or the added analyte of interest linked to the ECL moiety. Here also, the analyte of interest and the added analyte of interest are typically an antigen.

DEPR:
The invention can also be used in an immunometric format. The ECL moiety is linked to a binding partner of the analyte of interest. The analyte or an analog thereof is bound to a surface and accordingly the surface is capable of specifically binding with the binding partner. The surface can be the surface of a particle, membrane, strip, tube, etc. The analyte of interest can be an antigen.

DEPR:
Alternatively, the binding partner is a primary binding partner of the analyte of interest. A binding partner of the primary binding partner is a substance linked to the ECL moiety. Analyte or an analog thereof is bound to a surface and accordingly the surface is capable of specifically binding with the primary binding partner. The secondary binding partner linked to the ECL moiety specifically binds the primary binding partner. The analyte of interest is typically an antigen.

DEPR:
The invention can be used, for example, in sandwich assays as well. The analyte of interest can be an antigen. A substance linked to the ECL moiety is a binding partner of the analyte of interest. A binding partner not linked to the ECL moiety is bound to a surface and accordingly the surface is capable of binding to the analyte of interest.

DEPR:
Alternatively, the binding partner may be primary binding partner (BP-1) of the analyte of interest. A secondary binding partner of the primary binding partner is linked to the ECL moiety. The analyte of interest can be an antigen. Another primary binding partner (BP-2) which is not recognized by the secondary binding partner is bound to the surface and accordingly the surface is capable of binding to the analyte of interest. The surface and primary binding partner (BP-1) are capable of specifically binding the antigen and the secondary binding partner linked to the ECL moiety is capable of specifically binding the primary binding partner (BP-1). Also, the binding partner can be a primary binding partner (BP-1) of the analyte of interest. BP-1 is linked to the ECL moiety. Another primary binding partner (BP-1') which is different from BP-1 and binds the analyte of interest is used. A secondary binding partner of the primary binding partner BP-1' is bound to a surface and accordingly the surface is capable of binding the complex of analyte BP-1 and BP-1'.

DEPR:
The methods of the invention are advantageously used in nonseparation binding assays for use in hybridoma screening assay formats. The analyte of interest is a monoclonal antibody directed against a particular antigen. A binding partner of the analyte of interest is linked to the ECL moiety. Antigen is bound to a surface and accordingly the surface is capable of specifically binding with the analyte. The monoclonal antibody specifically binds the surface and the binding partner which is part of the ECL moiety specifically binds the monoclonal antibody.

DEPR:
Advantageously, the binding partner in the ECL moiety capable of specifically binding the monoclonal antibody is a polyclonal antibody, a monoclonal antibody, protein A, or protein G. In addition, that binding partner may be avidin, which can bind to a biotin-modified analyte.

DEPR:
Alternatively, the binding partner is a primary binding partner of the analyte of interest. A binding partner of the primary binding partner is linked to the ECL moiety. The analyte of interest is a monoclonal antibody directed against an antigen. Antigen is bound to a surface and accordingly the surface is capable of specifically binding with the monoclonal antibody. The monoclonal antibody specifically binds the surface, the primary binding partner specifically binds the monoclonal antibody, and the secondary binding partner in the ECL moiety specifically binds the primary binding partner.

CLPR:
22. A kit as defined in claim 11, which is adapted for detection of an analyte selected from the group consisting of whole cell or surface antigen, subcellular particle, virus, prion, viroid, antibody, antigen, hapten, fatty acid, nucleic acid, protein, lipoprotein, polysaccharide, lipopolysaccharide, glycoprotein, peptide, polypeptide, cellular metabolite, hormone, pharmacological agent, nonbiological polymer (preferably soluble), synthetic organic molecule, organometallic molecule, tranquilizer, barbituate, alkaloid, steroid, vitamin, amino acid, sugar, lectin, recombinant or derived protein, biotin, avidin, streptavidin, or inorganic molecule present in the sample.

CLPR:
27. A kit as defined in claim 26, which is adapted for detection of an analyte selected from the group consisting of a whole cell or surface antigen, subcellular particle, virus, prion, viroid, antibody, antigen, hapten, fatty acid, nucleic acid, protein, lipoprotein, polysaccharide, lipopolysaccharide, glycoprotein, peptide, polypeptide, cellular metabolite, hormone, pharmacological agent, nonbiological polymer (preferably soluble), synthetic organic molecule, organometallic molecule, tranquilizer, barbituate, alkaloid, steroid, vitamin, amino acid, sugar, lectin, recombinant or derived protein, biotin, avidin, streptavidin, or inorganic molecule present in the sample.

CLPV:
which kit consists essentially of (i) a metal chelate which, when oxidized by exposure to an effective amount of electrochemical energy, is capable of being converted to an excited state from which electrochemical radiation is emitted upon exposure of the excited metal chelate to conditions sufficient to induce said emission, (ii) an amine or an amine moiety which, when oxidized by exposure to an effective amount of electrochemical energy, forms a strong reducing agent, and (iii) an electrolyte capable of functioning as a medium in which said chelate and said amine or amine moiety can be oxidized by exposure to electrochemical energy and (iv) at least one substance selected from the group consisting of (a) additional analyte of

interest or an analog of the analyte of interest, (b) a binding partner of the analyte of interest or its said analog, and a reactive component capable of binding with substance (a) or (b).

ORPL:
Faulkner et al., Electroanalytical Chemistry, A.J. Bard (Ed.), vol. 10, Marcel Dekker, N.Y., 1977, Ch. 1.

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Document Number 6

Entry 6 of 9 File: USPT Jul 14, 1998

DOCUMENT-IDENTIFIER: US 5779976 A
TITLE: Apparatus for improved luminescence assays

INNM:
Massey; Richard J.

INZZ:
Massey; Richard J.

ASNM:
IGEN International, Inc.

ASZZ:
IGEN International, Inc.

BSPR:
Thus, U.S. 89/04,919 is directed to methods for the detection of an analyte of interest in a sample, which method includes the steps of (1) forming a composition comprising (a) a sample suspected of containing an analyte of interest, (b) an assay-performance-substance selected from the group consisting of (i) analyte of interest or analog of the analyte of interest, (ii) a binding partner of the analyte of interest or its said analog, and (iii) a reactive component capable of binding with (i) or (ii), wherein one of said substances is linked to a label compound having a chemical moiety capable of being induced to luminesce, and (c) a plurality of suspended particles capable of specifically binding with the analyte and/or a substance defined in (b) (i), (ii), or (iii); (2) incubating the composition to form a complex which includes a particle and said label compound; (3) inducing the label compound to luminesce; and (4) measuring the luminescence emitted by the composition to detect the presence of the analyte of interest in the sample. Those same methods may be used to quantify the amount of analyte in a sample by comparing the luminescence of the assay composition to the luminescence of a composition containing a known amount of analyte.

BSPR:
Analogs of the analyte of interest, which may be natural or synthetic, are compounds which have binding properties comparable to the analyte, but include compounds of higher or lower binding capability as well. Binding partners suitable for use in the present invention are well-known. Examples are antibodies, enzymes, nucleic acids, lectins, cofactors and receptors. The reactive components capable of binding with the analyte or its analog and/or with a binding partner thereof may be a second antibody or a protein such as Protein A or Protein G or may be avidin or biotin or another component known in the art to enter into binding reactions.

BSPR:
Advantageously, the luminescence arises from electrochemiluminescence (ECL) induced by exposing the label compound, whether bound or unbound to specific binding partners, to a voltammetric working

electrode. The ECL reactive mixture is controllably triggered to emit light by a voltage impressed on the working electrode at a particular time and in a particular manner to generate light. Although the emission of visible light is an advantageous feature the composition or system may emit other types of electromagnetic radiation, such as infrared or ultraviolet light, X-rays, microwaves, etc. Use of the terms "electrochemiluminescence," "electrochemiluminescent" "electrochemiluminescence" "luminescence," "luminescent," and "luminesce" includes the emission of light and other forms of electromagnetic radiation.

BSPR:
The term "ECL moiety," "metal-containing ECL moiety" "label," "label compound," and "label substance," are used interchangeably. It is within the scope of the invention for the species termed "ECL moiety," "metal-containing ECL moiety," "organometallic," "metal chelate," "transition metal chelate" "rare earth metal chelate," "label compound," "label substance" and "label" to be linked to molecules such as an analyte or an analog thereof, a binding partner of the analyte or an analog thereof, and further binding partners of such aforementioned binding partner, or a reactive component capable of binding with the analyte, an analog thereof or a binding partner as mentioned above. The above-mentioned species can also be linked to a combination of one or more binding partners and/or one or more reactive components. Additionally, the aforementioned species can also be linked to an analyte or its analog bound to a binding partner, a reactive component, or a combination of one or more binding partners and/or one or more reactive components. It is also within the scope of the invention for a plurality of the aforementioned species to be bound directly, or through other molecules as discussed above, to an analyte or its analog. For purposes of brevity, these ligands are referred to as an assay-performance-substance.

DEPR:
Typical analytes of interest are a whole cell or surface antigen, subcellular particle, virus, prion, viroid, antibody, antigen, hapten, fatty acid, nucleic acid, protein, lipoprotein, polysaccharide, lipopolysaccharide, glycoprotein, peptide, polypeptide, cellular metabolite, hormone, pharmacological agent, synthetic organic molecule, organometallic molecule, tranquilizer, barbiturate, alkaloid, steroid, vitamin, amino acid, sugar, lectin, recombinant or derived protein, biotin, avidin, streptavidin, or inorganic molecule present in the sample. Typically, the analyte of interest is present at a concentration of 10.sup.-3 molar or less, for example, as low as 10.sup.-12 molar or lower.

DEPR:
The assay-performance-substance which is combined with the sample containing the analyte of interest contains at least one substance selected from the group consisting of (i) added analyte of interest or its analog, as defined above, (ii) a binding partner of the analyte of interest or its said analog, and (iii) a reactive component, as defined above, capable of binding with (i) or (ii), wherein one of said substances is linked to a compound or moiety, e.g. an ECL moiety capable of being induced to luminesce. The labeled substance may be a whole cell or surface antigen, a subcellular particle, virus, prion, viroid, antibody, antigen, hapten, lipid, fatty acid, nucleic acid, polysaccharide, protein, lipoprotein, lipopolysaccharide, glycoprotein, peptide, polypeptide, cellular metabolite, hormone, pharmacological agent, tranquilizer, barbiturate, alkaloid, steroid, vitamin, amino acid, sugar, nonbiological polymer (preferably soluble), lectin, recombinant or derived protein, synthetic organic molecule, organometallic molecule, inorganic molecule, biotin, avidin or streptavidin. In one embodiment, the reagent is an electrochemiluminescent moiety conjugated to an antibody, antigen, nucleic acid, hapten, small nucleotide sequence, oligomer, ligand, enzyme, or biotin, avidin, streptavidin, Protein A, Protein G, or complexes thereof, or other

secondary binding partner capable of binding to a primary binding partner through protein interactions.

DEPR:
Analogs of the analyte of interest, which can be natural or synthetic, are typically compounds which have binding properties comparable to the analyte, but can also be compounds of higher or lower binding capability. The reactive components capable of binding with the analyte or its analog, and/or with a binding partner thereof, and through which the ECL moiety can be linked to the analyte, is suitably a second antibody or a protein such as Protein A or Protein G, or avidin or biotin or another component known in the art to enter into binding reactions.

DEPR:
The invention is also directed to reagent compositions. Broadly, the reagent compositions may be any one of the components of the assay systems of the invention, i.e., (a) electrolyte, (b) label compound containing an ECL moiety, (c) particles, including magnetically responsive particles, (d) analyte of interest or an analog of the analyte of interest, (e) a binding partner of the analyte of interest or of its analog, (f) a reactive component capable of reacting with (d) or (e), (g) a reductant, or (h) an electrochemiluminescence-reaction enhancer. The reagents may be combined with one another for convenience of use, i.e., two component, three component, and higher multiple component mixtures may be prepared, provided that the components are not reactive with one another during storage so as to impair their function in the intended assay. Desirably, the reagents are two-component or multicomponent mixtures which contain particles as well as one or more other components.

URNM:
Bard et al.

Document Number 7

Entry 7 of 9 File: USPT Jun 23, 1998

DOCUMENT-IDENTIFIER: US 5770459 A
TITLE: Methods and apparatus for improved luminescence assays using particle concentration, electrochemical generation of chemiluminescence detection

INNM:
Massey; Richard J.

INZZ:
Massey; Richard J.

ASNM:
IGEN International, Inc.

ASZZ:
IGEN International, Inc.

BSPR:
Thus, U.S. 89/04919 is directed to methods for the detection of an analyte of interest in a sample, which method includes the steps of (1) forming a composition comprising (a) a sample suspected of containing an analyte of interest, (b) an assay-performance-substance selected from the group consisting of (i) analyte of interest or analog of the analyte of interest, (ii) a binding partner of the analyte of interest or its said analog, and (iii) a reactive component capable of binding with (i) or (ii), wherein one of said substances is linked to a label compound having a chemical moiety capable of being induced to luminesce, and (c) a plurality of suspended particles capable of specifically binding with the analyte and/or a substance defined in (b)(i), (ii), or (iii); (2) incubating the composition to form a complex which includes a particle and said label compound; (3) inducing the label compound to luminesce; and (4) measuring the luminescence emitted by the composition to detect the presence of the analyte of interest in the sample. Those same methods may be used to quantify the amount of analyte in a sample by comparing the luminescence of the assay composition to the luminescence of a composition containing a known amount of analyte.

BSPR:
Analogs of the analyte of interest, which may be natural or synthetic, are compounds which have binding properties comparable to the analyte, but include compounds of higher or lower binding capability as well. Binding partners suitable for use in the present invention are well-known. Examples are antibodies, enzymes, nucleic acids, lectins, cofactors and receptors. The reactive components capable of binding with the analyte or its analog and/or with a binding partner thereof may be a second antibody or a protein such as Protein A or Protein G or may be avidin or biotin or another component known in the art to enter into binding reactions.

BSPR:
Advantageously, the luminescence arises from electrochemiluminescence

(ECL) induced by exposing the label compound, whether bound or unbound to specific binding partners, to a voltametric working electrode. The ECL reactive mixture is controllably triggered to emit light by a voltage impressed on the working electrode at a particular time and in a particular manner to generate light. Although the emission of visible light is an advantageous feature the composition or system may emit other types of electromagnetic radiation, such as infrared or ultraviolet light, X-rays, microwaves, etc. Use of the terms "electrochemiluminescence," "electrochemiluminescent," "luminescence," "luminescent," and "luminesce" includes the emission of light and other forms of electromagnetic radiation.

BSPR:
Specific binding assays, e.g. immunoassays, using chemiluminescent detection use one of the reactants as a label attached to one of the binding partners. In such assays, the reactants are generally called the label and the trigger and react according to the equation:

BSPR:
The term "chemiluminescent moiety," "label," "label compound," and "label substance," are used interchangeably. It is within the scope of the invention for the species termed "chemiluminescent moiety," "label compound," "label substance" and "label" to be linked to molecules such as an analyte or an analog thereof, a binding partner of the analyte or an analog thereof, and further binding partners of such aforementioned binding partner, or a reactive component capable of binding with the analyte, an analog thereof or a binding partner as mentioned above. The above-mentioned species can also be linked to a combination of one or more binding partners and/or one or more reactive components. Additionally, the aforementioned species can also be linked to an analyte or its analog bound to a binding partner, a reactive component, or a combination of one or more binding partners and/or one or more reactive components. It is also within the scope of the invention for a plurality of the aforementioned species to be bound directly, or through other molecules as discussed above, to an analyte or its analog. For purposes of brevity, these ligands are referred to as an assay-performance-substance.

DEPR:
Typical analytes of interest are a whole cell or surface antigen, subcellular particle, virus, prion, viroid, antibody, antigen, hapten, fatty acid, nucleic acid, protein, lipoprotein, polysaccharide, lipopolysaccharide, glycoprotein, peptide, polypeptide, cellular metabolite, hormone, pharmacological agent, synthetic organic molecule, organometallic molecule, tranquilizer, barbiturate, alkaloid, steroid, vitamin, amino acid, sugar, lectin, recombinant or derived protein, biotin, avidin, streptavidin, or inorganic molecule present in the sample. Typically, the analyte of interest is present at a concentration of 10.sup.-3 molar or less, for example, as low as 10.sup.-12 molar or lower.

DEPR:
The assay-performance-substance which is combined with the sample containing the analyte of interest contains at least one substance selected from the group consisting of (i) added analyte of interest or its analog, as defined above, (ii) a binding partner of the analyte of interest or its said analog, and (iii) a reactive component, as defined above, capable of binding with (i) or (ii), wherein one of said substances is linked to a compound or moiety, e.g. a chemiluminescent moiety capable of being induced to luminesce. The labeled substance may be a whole cell or surface antigen, a subcellular particle, virus, prion, viroid, antibody, antigen, hapten, lipid, fatty acid, nucleic acid, polysaccharide, protein, lipoprotein, lipopolysaccharide, glycoprotein, peptide, polypeptide, cellular metabolite, hormone, pharmacological agent, tranquilizer, barbiturate, alkaloid, steroid, vitamin, amino acid, sugar, nonbiological polymer (preferably soluble), lectin, recombinant or derived protein, synthetic organic molecule, organometallic molecule,

inorganic molecule, biotin, avidin or streptavidin. In one embodiment, the reagent is a chemiluminescent moiety conjugated to an antibody, antigen, nucleic acid, hapten, small nucleotide sequence, oligomer, ligand, enzyme, or biotin, avidin, streptavidin, Protein A, Protein G, or complexes thereof, or other secondary binding partner capable of binding to a primary binding partner through protein interactions.

DEPR:
Analogs of the analyte of interest, which can be natural or synthetic, are typically compounds which have binding properties comparable to the analyte, but can also be compounds of higher or lower binding capability. The reactive components capable of binding with the analyte or its analog, and/or with a binding partner thereof, and through which the chemiluminescent moiety can be linked to the analyte, is suitably a second antibody or a protein such as Protein A or Protein G, or avidin or biotin or another component known in the art to enter into binding reactions.

DEPR:
The invention is also directed to reagent compositions. Broadly, the reagent compositions may be any one of the components of the assay systems of the invention, i.e., (a) electrolyte, (b) label compound containing a chemiluminescent moiety, (c) particles, including magnetically responsive particles, (d) analyte of interest or an analog of the analyte of interest, (e) a binding partner of the analyte of interest or of its analog, (f) a reactive component capable of reacting with (d) or (e), (g) a trigger precursor molecule, or (h) a chemiluminescence-reaction enhancer. The reagents may be combined with one another for convenience of use, i.e., two component, three component, and higher multiple component mixtures may be prepared, provided that the components are not reactive with one another during storage so as to impair their function in the intended assay. Desirably, the reagents are two-component or multicomponent mixtures which contain particles as well as one or more other components.

CLPX:
(2) one or more binding partners of said analyte or said analogue: and

CLPX:
(2) one or more binding partners of said analyte or said analogue; and

CLPX:
(2) one or more binding partners of said analyte or said analogue; and

CLPX:
(2) one or more binding partners of said analyte or said analogue; and

CLPX:
(2) one or more binding partners of said analyte or said analogue; and

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Document Number 8

Entry 8 of 9 File: USPT May 5, 1998

DOCUMENT-IDENTIFIER: US 5746974 A
TITLE: Apparatus for improved luminescence assays using particle concentration, electrochemical generation of chemiluminescence and chemiluminescence detection

INNM:
Massey; Richard J.

INZZ:
Massey; Richard J.

ASNM:
IGEN International, Inc.

ASZZ:
IGEN International, Inc.

BSPR:
Thus, U.S. 89/04919 is directed to methods for the detection of an analyte of interest in a sample, which method includes the steps of (1) forming a composition comprising (a) a sample suspected of containing an analyte of interest, (b) an assay-performance-substance selected from the group consisting of (i) analyte of interest or analog of the analyte of interest, (ii) a binding partner of the analyte of interest or its said analog, and (iii) a reactive component capable of binding with (i) or (ii), wherein one of said substances is linked to a label compound having a chemical moiety capable of being induced to luminesce, and (c) a plurality of suspended particles capable of specifically binding with the analyte and/or a expect that the luminescence from free chemiluminescent moieties would be absorbed, scattered, or otherwise suffer interference from the microparticulate matter.

BSPR:
Thus, U.S. 89/04919 is directed to methods for the detection of an analyte of interest in a sample, which method includes the steps of (1) forming a composition comprising (a) a sample suspected of containing an analyte of interest, (b) an assay-performance-substance selected from the group consisting of (i) analyte of interest or analog of the analyte of interest, (ii) a binding partner of the analyte of interest or its said analog, and (iii) a reactive component capable of binding with (i) or (ii), wherein one of said substances is linked to a label compound having a chemical moiety capable of being induced to luminesce, and (c) a plurality of suspended particles capable of specifically binding with the analyte and/or a substance defined in (b)(i), (ii), or (iii); (2) incubating the composition to form a complex which includes a particle and said label compound; (3) inducing the label compound to luminesce; and (4) measuring the luminescence emitted by the composition to detect the presence of the analyte of interest in the sample. Those same methods may be used to quantify the amount of analyte in a sample by comparing the luminescence of the assay composition to the luminescence of a composition containing a known amount of analyte.

BSPR:
Analogs of the analyte of interest, which may be natural or synthetic, are compounds which have binding properties comparable to the analyte, but include compounds of higher or lower binding capability as well. Binding partners suitable for use in the present invention are well-known. Examples are antibodies, enzymes, nucleic acids, lectins, cofactors and receptors. The reactive components capable of binding with the analyte or its analog and/or with a binding partner thereof may be a second antibody or a protein such as Protein A or Protein G or may be avidin or biotin or another component known in the art to enter into binding reactions.

BSPR:
Advantageously, the luminescence arises from electrochemiluminescence (ECL) induced by exposing the label compound, whether bound or unbound to specific binding partners, to a voltametric working electrode. The ECL reactive mixture is controllably triggered to emit light by a voltage impressed on the working electrode at a particular time and in a particular manner to generate light. Although the emission of visible light is an advantageous feature the composition or system may emit other types of electromagnetic radiation, such as infrared or ultraviolet light, X-rays, microwaves, etc. Use of the terms "electrochemiluminescence," "electrochemiluminescent," "luminescence," "luminescent," and "luminesce" includes the emission of light and other forms of electromagnetic radiation.

BSPR:
Specific binding assays, e.g. immunoassays, using chemiluminescent detection use one of the reactants as a label attached to one of the binding partners. In such assays, the reactants are generally called the label and the trigger and react according to the equation:

BSPR:
The term "chemiluminescent moiety," "label," "label compound," and "label substance," are used interchangeably. It is within the scope of the invention for the species termed "chemiluminescent moiety," "label compound," "label substance" and "label" to be linked to molecules such as an analyte or an analog thereof, a binding partner of the analyte or an analog thereof, and further binding partners of such aforementioned binding partner, or a reactive component capable of binding with the analyte, an analog thereof or a binding partner as mentioned above. The above-mentioned species can also be linked to a combination of one or more binding partners and/or one or more reactive components. Additionally, the aforementioned species can also be linked to an analyte or its analog bound to a binding partner, a reactive component, or a combination of one or more binding partners and/or one or more reactive components. It is also within the scope of the invention for a plurality of the aforementioned species to be bound directly, or through other molecules as discussed above, to an analyte or its analog. For purposes of brevity, these ligands are referred to as an assay-performance-substance.

DEPR:
Typical analytes of interest are a whole cell or surface antigen, subcellular particle, virus, prion, viroid, antibody, antigen, hapten, fatty acid, nucleic acid, protein, lipoprotein, polysaccharide, lipopolysaccharide, glycoprotein, peptide, polypeptide, cellular metabolite, hormone, pharmacological agent, synthetic organic molecule, organometallic molecule, tranquilizer, barbiturate, alkaloid, steroid, vitamin, amino acid, sugar, lectin, recombinant or derived protein, biotin, avidin, streptavidin, or inorganic molecule present in the sample. Typically, the analyte of interest is present at a concentration of 10.sup.-3 molar or less, for example, as low as 10.sup.-12 molar or lower.

DEPR:
The assay-performance-substance which is combined with the sample

containing the analyte of interest contains at least one substance selected from the group consisting of (i) added analyte of interest or its analog, as defined above, (ii) a binding partner of the analyte of interest or its said analog, and (iii) a reactive component, as defined above, capable of binding with (i) or (ii), wherein one of said substances is linked to a compound or moiety, e.g. a chemiluminescent moiety capable of being induced to luminesce. The labeled substance may be a whole cell or surface antigen, a subcellular particle, virus, prion, viroid, antibody, antigen, hapten, lipid, fatty acid, nucleic acid, polysaccharide, protein, lipoprotein, lipopolysaccharide, glycoprotein, peptide, polypeptide, cellular metabolite, hormone, pharmacological agent, tranquilizer, barbiturate, alkaloid, steroid, vitamin, amino acid, sugar, nonbiological polymer (preferably soluble), lectin, recombinant or derived protein, synthetic organic molecule, organometallic molecule, inorganic molecule, biotin, avidin or streptavidin. In one embodiment, the reagent is a chemiluminescent moiety conjugated to an antibody, antigen, nucleic acid, hapten, small nucleotide sequence, oligomer, ligand, enzyme, or biotin, avidin, streptavidin, Protein A, Protein G, or complexes thereof, or other secondary binding partner capable of binding to a primary binding partner through protein interactions.

DEPR:
Analogs of the analyte of interest, which can be natural or synthetic, are typically compounds which have binding properties comparable to the analyte, but can also be compounds of higher or lower binding capability. The reactive components capable of binding with the analyte or its analog, and/or with a binding partner thereof, and through which the chemiluminescent moiety can be linked to the analyte, is suitably a second antibody or a protein such as Protein A or Protein G, or avidin or biotin or another component known in the art to enter into binding reactions.

DEPR:
The invention is also directed to reagent compositions. Broadly, the reagent compositions may be any one of the components of the assay systems of the invention, i.e., (a) electrolyte, (b) label compound containing a chemiluminescent moiety, (c) particles, including magnetically responsive particles, (d) analyte of interest or an analog of the analyte of interest, (e) a binding partner of the analyte of interest or of its analog, (f) a reactive component capable of reacting with (d) or (e), (g) a trigger precursor molecule, or (h) a chemiluminescence-reaction enhancer. The reagents may be combined with one another for convenience of use, i.e., two component, three component, and higher multiple component mixtures may be prepared, provided that the components are not reactive with one another during storage so as to impair their function in the intended assay. Desirably, the reagents are two-component or multicomponent mixtures which contain particles as well as one or more other components.

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Document Number 9

Entry 9 of 9 File: USPT Jan 6, 1998

DOCUMENT-IDENTIFIER: US 5705402 A
TITLE: Method and apparatus for magnetic microparticulate based luminescence assay including plurality of magnets

INNM:
Massey; Richard J.

INZZ:
Massey; Richard J.

ASNM:
Igen International, Inc.

ASZZ:
Igen International, Inc.

BSPR:
Thus, U.S. Ser. No. 89/04919 is directed to methods for the detection of an analyte of interest in a sample, which method includes the steps of (1) forming a composition comprising (a) a sample suspected of containing an analyte of interest, (b) an assay-performance-substance selected from the group consisting of (i) analyte of interest or analog of the analyte of interest, (ii) a binding partner of the analyte of interest or its said analog, and (iii) a reactive component capable of binding with (i) or (ii), wherein one of said substances is linked to a label compound having a chemical moiety capable of being induced to luminesce, and (c) a plurality of suspended particles capable of specifically binding with the analyte and/or a substance defined in (b)(i), (ii), or (iii); (2) incubating the composition to form a complex which includes a particle and said label compound; (3) inducing the label compound to luminesce; and (4) measuring the luminescence emitted by the composition to detect the presence of the analyte of interest in the sample. Those same methods may be used to quantify the amount of analyte in a sample by comparing the luminescence of the assay composition to the luminescence of a composition containing a known amount of analyte.

BSPR:
Analogs of the analyte of interest, which may be natural or synthetic, are compounds which have binding properties comparable to the analyte, but include compounds of higher or lower binding capability as well. Binding partners suitable for use in the present invention are well-known. Examples are antibodies, enzymes, nucleic acids, lectins, cofactors and receptors. The reactive components capable of binding with the analyte or its analog and/or with a binding partner thereof may be a second antibody or a protein such as Protein A or Protein G or may be avidin or biotin or another component known in the art to enter into binding reactions.

BSPR:
Advantageously, the luminescence arises from electrochemiluminescence

(ECL) induced by exposing the label compound, whether bound or unbound to specific binding partners, to a voltammetric working electrode. The ECL reactive mixture is controllably triggered to emit light by a voltage impressed on the working electrode at a particular time and in a particular manner to generate light. Although the emission of visible light is an advantageous feature the composition or system may emit other types of electromagnetic radiation, such as infrared or ultraviolet light, X-rays, microwaves, etc. Use of the terms "electrochemiluminescence," "electrochemiluminescent," "luminescence," "luminescent," and "luminesce" includes the emission of light and other forms of electromagnetic radiation.

BSPR:
The term "ECL moiety," "metal-containing ECL moiety" "label," "label compound," and "label substance," are used interchangeably. It is within the scope of the invention for the species termed "ECL moiety," "metal-containing ECL moiety," "organo-metallic," "metal chelate," "transition metal chelate" "rare earth metal chelate," "label compound," "label substance" and "label" to be linked to molecules such as an analyte or an analog thereof, a binding partner of the analyte or an analog thereof, and further binding partners of such aforementioned binding partner, or a reactive component capable of binding with the analyte, an analog thereof or a binding partner as mentioned above. The above-mentioned species can also be linked to a combination of one or more binding partners and/or one or more reactive components. Additionally, the aforementioned species can also be linked to an analyte or its analog bound to a binding partner, a reactive component, or a combination of one or more binding partners and/or one or more reactive components. It is also within the scope of the invention for a plurality of the aforementioned species to be bound directly, or through other molecules as discussed above, to an analyte or its analog. For purposes of brevity, these ligands are referred to as an assay-performance-substance.

DEPR:
Typical analytes of interest are a whole cell or surface antigen, subcellular particle, virus, prion, viroid, antibody, antigen, hapten, fatty acid, nucleic acid, protein, lipoprotein, polysaccharide, lipopolysaccharide, glycoprotein, peptide, polypeptide, cellular metabolite, hormone, pharmacological agent, synthetic organic molecule, organometallic molecule, tranquilizer, barbiturate, alkaloid, steroid, vitamin, amino acid, sugar, lectin, recombinant or derived protein, biotin, avidin, streptavidin, or inorganic molecule present in the sample. Typically, the analyte of interest is present at a concentration of 10.sup.-3 molar or less, for example, as low as 10.sup.-12 molar or lower.

DEPR:
The assay-performance-substance which is combined with the sample containing the analyte of interest contains at least one substance selected from the group consisting of (i) added analyte of interest or its analog, as defined above, (ii) a binding partner of the analyte of interest or its said analog, and (iii) a reactive component, as defined above, capable of binding with (i) or (ii), wherein one of said substances is linked to a compound or moiety, e.g. an ECL moiety capable of being induced to luminesce. The labeled substance may be a whole cell or surface antigen, a subcellular particle, virus, prion, viroid, antibody, antigen, hapten, lipid, fatty acid, nucleic acid, polysaccharide, protein, lipoprotein, lipopolysaccharide, glycoprotein, peptide, polypeptide, cellular metabolite, hormone, pharmacological agent, tranquilizer, barbiturate, alkaloid, steroid, vitamin, amino acid, sugar, nonbiological polymer (preferably soluble), lectin, recombinant or derived protein, synthetic organic molecule, organometallic molecule, inorganic molecule, biotin, avidin or streptavidin. In one embodiment, the reagent is an electrochemiluminescent moiety conjugated to an antibody, antigen, nucleic acid, hapten, small nucleotide sequence, oligomer, ligand, enzyme, or biotin, avidin,

streptavidin, Protein A, Protein G, or complexes thereof, or other secondary binding partner capable of binding to a primary binding partner through protein interactions.

DEPR:
Analogs of the analyte of interest, which can be natural or synthetic, are typically compounds which have binding properties comparable to the analyte, but can also be compounds of higher or lower binding capability. The reactive component capable of binding with the analyte or its analog, and/or with a binding partner thereof, and through which the ECL moiety can be linked to the analyte, is suitably a second antibody or a protein such as Protein A or Protein G, or avidin or biotin or another component known in the art to enter into binding reactions.

DEPR:
In the practice of the method and use of the apparatus of the invention, reagent compositions are used. The reagent compositions are the components of the assay systems of the invention, i.e., (a) electrolyte, (b) label compound containing an ECL moiety, (c) particles, including magnetically responsive particles, (d) analyte of interest or an analog of the analyte of interest, (e) a binding partner of the analyte of interest or of its analog, (f) a reactive component capable of reacting with (d) or (e), (g) a reductant, or (h) an electrochemiluminescence-reaction enhancer. The reagents may be combined with one another for convenience of use, i.e., two component, three component, and higher multiple component mixtures may be prepared, provided that the components are not reactive with one another during storage so as to impair their function in the intended assay. Desirably, the reagents are two-component or multicomponent mixtures which contain particles as well as one or more other components.

CLPW:
(iii) a plurality of magnetically responsive suspended particles to which are bound a binding partner of said analyte and/or said assay-performance-substance;

CLPX:
(2) a binding partner of said analyte or said analogue;

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☐ 1. Document ID: US 5976887 A

Entry 1 of 53 File: USPT Nov 2, 1999

US-PAT-NO: 5976887
DOCUMENT-IDENTIFIER: US 5976887 A

TITLE: Electrochemiluminescence assays based on interactions with soluble metal ions and diaminoaromatic ligands

DATE-ISSUED: November 2, 1999

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Bruno; John G.	San Antonio	TX	N/A	N/A
Cornette; Jimmy C.	Niceville	FL	N/A	N/A

US-CL-CURRENT: 436/80; 252/389.5, 252/389.53, 252/389.54, 252/390, 252/400.5, 252/400.53, 252/400.54, 252/401, 252/405, 436/106, 436/111, 436/166, 436/172, 436/73, 436/74, 436/83, 436/84

ABSTRACT:

A novel electrochemiluminescent (ECL) reaction between diaminoaromatic ligands and soluble metal ions, specifically reactions between aminoaromatic ligands, such as 2,4-diaminotoluene (2,4,DAT), 3,4-diaminotoluene (3,4,DAT) and 2,3-diaminonaphthalene (2,3-DAN) and metal ions such as Au(I), Cu(II), Cr(VI), Fe(III), Ru)III), Se(IV) and V(V). Such reactions form the basis for ECL assays in detection of various substances, such as the reactants. The ECL interaction between these substances can also form the basis for binding methods in the detection of other substances, such as nucleic acids and antibodies wherein the metal ion ligand ECL complex may be used as a label. The ECL assays are considered useful for carrying out field and laboratory analyses for the detection of TNT breakdown products and toxic metals in wastewater streams, soil, and ground water supplies. In view of the formation of such ECL complexes being dependent on molecular size, further uses are contemplated for measuring atomic size or intermolecular distances of the complexes formed.
23 Claims, 14 Drawing figures
Exemplary Claim Number: 10
Number of Drawing Sheets: 13

☐ 2. Document ID: US 5962218 A

Entry 2 of 53 File: USPT Oct 5, 1999

US-PAT-NO: 5962218
DOCUMENT-IDENTIFIER: US 5962218 A

TITLE: Methods and apparatus for improved luminescence assays

DATE-ISSUED: October 5, 1999

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Leland; Jonathan K.	Laurel	MD	N/A	N/A
Shah; Haresh P.	Gaithersburg	MD	N/A	N/A
Kenten; John H.	Gaithersburg	MD	N/A	N/A
Goodman; Jack E.	Arlington	VA	N/A	N/A
Lowke; George E.	Laytonsville	MD	N/A	N/A
Blackburn; Gary F.	Gaithersburg	MD	N/A	N/A
Massey; Richard J.	Rockville	MD	N/A	N/A

US-CL-CURRENT: 435/6; 435/7.1, 436/501, 436/518, 436/526, 436/528, 436/530, 436/531, 436/534, 436/544

ABSTRACT:

The invention relates to methods, apparatus, reagents, and kits for performing a binding assay for an analyte of interest present in a sample based upon electrochemiluminescence at an electrode of interest. In the method, reagents and kits particles can be employed; for instance, for settling upon the electrode surface by gravity, centrifugation or magnetic attraction. The apparatus can include a magnet for generating a magnetic field in a region proximate the electrode.
45 Claims, 26 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 16

☐ 3. Document ID: US 5952462 A

Entry 3 of 53 File: USPT Sep 14, 1999

US-PAT-NO: 5952462
DOCUMENT-IDENTIFIER: US 5952462 A

TITLE: Transition state analogs

DATE-ISSUED: September 14, 1999

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Powell; Michael J.	Gaithersburg	MD	N/A	N/A
Titmas; Richard C.	Rockville	MD	N/A	N/A
Massey; Richard J.	Rockville	MD	N/A	N/A

US-CL-CURRENT: 530/317; 530/323, 530/328, 530/329, 530/330, 530/331, 530/332, 530/345 , 530/403, 540/460, 540/487, 540/522, 544/224, 548/111, 556/19, 556/406, 558/44, 558/48

ABSTRACT:

Antigens capable of eliciting antibodies which can catalyze chemical reactions, in particular, the cleavage or formation of a peptide linkage, comprising a hapten or a hapten and a suitable carrier molecule are disclosed. Haptens include, among others, silicon and boron containing compounds. Antibodies which are catalytically active for chemical reactions, in particular, the cleavage or formation of a selected peptide linkage or an ester bond, and which are elicited by such antigens are disclosed as well as methods for producing the antibodies and methods for catalyzing the cleavage or formation of a peptide linkage or in ester bond in a molecule.
25 Claims, 24 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 30

4. Document ID: US 5945344 A

Entry 4 of 53 File: USPT Aug 31, 1999

US-PAT-NO: 5945344
DOCUMENT-IDENTIFIER: US 5945344 A

TITLE: Electrochemiluminescence method

DATE-ISSUED: August 31, 1999

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Hayes; Stephanie A.	Gaithersburg	MD	N/A	N/A
Leland; Jonathan K.	Silver Spring	MD	N/A	N/A
Talley; David B.	Olney	MD	N/A	N/A

US-CL-CURRENT: 436/172; 250/361C, 422/52

ABSTRACT:

The invention is a method for conducting an electrochemiluminescent assay that includes contacting a sample containing an analyte of interest with a first electrical waveform, followed by contacting the sample with a second electrical waveform that has been modulated in an amount derived from a pre-determined gain extension factor.
50 Claims, 6 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 6

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Image

☐ 5. Document ID: US 5935779 A

Entry 5 of 53 File: USPT Aug 10, 1999

US-PAT-NO: 5935779
DOCUMENT-IDENTIFIER: US 5935779 A

TITLE: Methods for improved particle electrochemiluminescence assay

DATE-ISSUED: August 10, 1999

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Massey; Richard J.	Rockville	MD	N/A	N/A
Leland; Jonathan K.	Laurel	MD	N/A	N/A
Shah; Haresh P.	Pleasant Hill	CA	N/A	N/A
Kenten; John H.	Gaithersburg	MD	N/A	N/A
Goodman; Jack E.	Arlington	VA	N/A	N/A
Lowke; George E.	Laytonsville	MD	N/A	N/A
Namba; Yuzaburo	Tsukuba	N/A	N/A	JPX
Blackburn; Gary F.	Gaithersburg	MD	N/A	N/A

US-CL-CURRENT: 435/6; 435/7.1, 436/518, 436/526, 436/528, 436/530, 436/531, 436/534, 436/544

ABSTRACT:

The invention relates to methods of performing a binding assay for an analyte of interest present in a sample based upon electrochemiluminescence at an electrode of interest. Particles are employed in the method, which are then collected in a zone at which electrochemiluminescence can be induced, wherein the amount of induced electrochemilurninescence is related to the amount of analyte in the sample.
3 Claims, 24 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 15

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Image

☐ 6. Document ID: US 5900237 A

Entry 6 of 53 File: USPT May 4, 1999

US-PAT-NO: 5900237
DOCUMENT-IDENTIFIER: US 5900237 A

TITLE: Catalytic antibodies which hydrolyze primary amides and methods for eliciting such antibodies

DATE-ISSUED: May 4, 1999

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Napper; Andrew D.	Hopkinton	MA	N/A	N/A
Titmas; Richard C.	North Potomac	MD	N/A	N/A
Martin; Mark T.	North Bethesda	MD	N/A	N/A
Hong; Wonpyo	Hockessin	DE	N/A	N/A

US-CL-CURRENT: 424/175.1; 424/94.1, 435/188.5

ABSTRACT:

Described and claimed are compounds of formula (I) wherein Y is a polypeptide, R.sub.1 is bonded to the N-terminus of Y and is hydrogen or a branched or linear, substituted or unsubstituted, C.sub.1-21 alkyl, alkene, or alkyne group, R.sub.2 is a side chain of a naturally occurring amino acid, and X is (a), (b), (c). Such compounds are useful as haptens and immunogens for the elicitation of antibodies which catalytically enhance the rate of formation or hydrolysis of primary amide bonds. Also described and claimed are methods employing the compounds and antibodies.
15 Claims, 14 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 14

☐ 7. Document ID: US 5888745 A

Entry 7 of 53 File: USPT Mar 30, 1999

US-PAT-NO: 5888745
DOCUMENT-IDENTIFIER: US 5888745 A

TITLE: Interference elimination reagent for the determination of an analyte using a metal complex capable of luminescence

DATE-ISSUED: March 30, 1999

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Eckert; Bernhard	Weilheim	N/A	N/A	DEX
Lenz; Helmut	Tutzing	N/A	N/A	DEX
Franken; Norbert	Starnberg	N/A	N/A	DEX
Josel; Hans-Peter	Weilheim	N/A	N/A	DEX
Ofenloch-Hahnle; Beatus	Polling	N/A	N/A	DEX

US-CL-CURRENT: 435/7.1; 435/6, 435/7.8, 435/7.92, 435/7.93, 435/7.94, 435/975, 436/172, 436/501, 436/518, 436/536, 436/537, 436/543, 436/546, 436/73

ABSTRACT:

The present invention concerns a method for the determination of an analyte in a sample liquid using a metal complex capable of luminescence as an analyte-specific marker group for the production of a measuring signal in which an unspecific metal complex is additionally added as an interference elimination reagent which has a structure that is chemically related to the marker group.
33 Claims, 9 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 6

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Image

☐ 8. Document ID: US 5866434 A

Entry 8 of 53 File: USPT Feb 2, 1999

US-PAT-NO: 5866434
DOCUMENT-IDENTIFIER: US 5866434 A

TITLE: Graphitic nanotubes in luminescence assays

DATE-ISSUED: February 2, 1999

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Massey; Richard J.	Rockville	MD	N/A	N/A
Martin; Mark T.	Bethesda	MD	N/A	N/A
Dong; Liwen	Rockville	MD	N/A	N/A
Lu; Ming	Lanham	MD	N/A	N/A
Fischer; Alan	Cambridge	MD	N/A	N/A
Jameison; Fabian	Gaithersburg	MD	N/A	N/A
Liang; Pam	Rockville	MD	N/A	N/A
Hoch; Robert	Hensonville	NY	N/A	N/A
Leland; Jonathan K.	Silver Spring	MD	N/A	N/A

US-CL-CURRENT: 436/526; 435/176, 435/182, 435/24, 435/26, 435/6, 435/7.4, 435/7.5, 435/7.92, 435/7.93, 435/7.94, 436/524, 436/535, 436/806, 530/391.1, 530/391.3, 530/391.5

ABSTRACT:

Graphitic nanotubes, which include tubular fullerenes (commonly called "buckytubes") and fibrils, which are functionalized by chemical substitution, are used as solid supports in electrogenerated chemiluminescence assays. The graphitic nanotubes are chemically modified with functional group biomolecules prior to use in an assay. Association of electrochemiluminescent ruthenium complexes with the functional group biomolecule-modified nanotubes permits detection of molecules including nucleic acids, antigens, enzymes, and enzyme substrates by multiple formats.
19 Claims, 13 Drawing figures
Exemplary Claim Number: 8
Number of Drawing Sheets: 12

FULL | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Image

☐ 9. Document ID: US 5858676 A

Entry 9 of 53 File: USPT Jan 12, 1999

US-PAT-NO: 5858676
DOCUMENT-IDENTIFIER: US 5858676 A

TITLE: Electrochemiluminescence of rare earth metal chelates

DATE-ISSUED: January 12, 1999

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Yang; Hongjun	Rockville	MD	N/A	N/A
Cairns; Nicholas	Gaithersburg	MD	N/A	N/A

US-CL-CURRENT: 435/6; 435/7.1, 435/7.2, 436/172, 436/501, 436/518, 436/537, 436/806, 436/82

ABSTRACT:

Luminescent chemical reagents that include complexes of rare earth metals with ligands such as aromatic heterocyclic nitrogen-containing compounds and semi-aromatic oxygen-containing compounds are used to detect small quantities of complex substances such as pharmaceuticals, metabolites, and microorganisms in complex sample mixtures.
15 Claims, 2 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 1

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Image

☐ 10. Document ID: US 5846485 A

Entry 10 of 53 File: USPT Dec 8, 1998

US-PAT-NO: 5846485
DOCUMENT-IDENTIFIER: US 5846485 A

TITLE: Electrochemiluminescent reaction utilizing amine-derived reductant

DATE-ISSUED: December 8, 1998

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Leland; Jonathan Kent	Laurel	MD	N/A	N/A
Powell; Michael Joseph	Gaithersburg	MD	N/A	N/A

US-CL-CURRENT: 422/52; 436/172, 436/800, 436/84

ABSTRACT:

A composition suitable for use in an ECL assay wherein electromagnetic radiation emitted by said composition is detected, which composition comprises (a) a metal-containing ECL moiety which, when oxidized by exposure to an effective amount of electrochemical energy, is capable of being converted to an excited state from which electromagnetic radiation is emitted upon exposure of the excited ECL moiety to conditions sufficient to induce said emission; (b) an amine or amine moiety which, when oxidized by exposure to an effective amount of electrochemical energy, forms a strong reducing agent in said composition; and (c) an electrolyte capable of functioning as a medium in which said ECL moiety and said amine or amine moiety can be oxidized by exposure to electrochemical energy.
30 Claims, 5 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 4

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Image

11. Document ID: US 5811236 A

Entry 11 of 53 File: USPT Sep 22, 1998

US-PAT-NO: 5811236
DOCUMENT-IDENTIFIER: US 5811236 A

TITLE: Electrochemiluminescent rhenium moieties and methods for their use

DATE-ISSUED: September 22, 1998

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Massey; Richard J.	Rockville	MD	N/A	N/A
Powell; Michael J.	Gaithersburg	MD	N/A	N/A
Dressick; Walter J.	Gaithersburg	MD	N/A	N/A
Leland; Jonathan K.	Gaithersburg	MD	N/A	N/A
Hino; Janel K.	Arlington	VA	N/A	N/A
Poonian; Mohindar S.	Gaithersburg	MD	N/A	N/A
Ciana; Leopoldo Della	Gaithersburg	MD	N/A	N/A

US-CL-CURRENT: 435/6; 435/252.1, 435/5, 435/7.1, 435/7.2, 435/7.9, 436/500, 436/537, 436/548, 514/2, 530/387.2, 536/24.3, 536/45, 536/46, 536/49, 546/2

ABSTRACT:

Electrochemiluminiscent moieties having the formula

[Re(P).sub.m (L.sup.1).sub.n (L.sup.2).sub.o (L.sup.3).sub.p (L.sup.4).sub.q (L.sup.5).sub.r (L.sup.6).sub.s].sub.t (B).sub.u

wherein

P is a polydentate ligand of Re;

L.sup.1, L.sup.2, L.sup.3, L.sup.4, L.sup.5 and L.sup.6 are ligands of Re, each of which may be the same as or different from each other ligand;

B is a substance which is a ligand of Re or is conjugated to one or more of P, L.sup.1, L.sup.2, L.sup.3, L.sup.4, L.sup.5 or L.sup.6 ;

m is an integer equal to or greater than 1;

each of n, o, p, q, r and s is zero or an integer;

t is an integer equal to or greater than 1; and

u is an integer equal to or greater than 1;

P, L.sup.1, L.sup.2, L.sup.3, L.sup.4, L.sup.5, L.sup.6 and B being of such composition and number that the chemical moiety can be induced to emit electromagnetic radiation and the total number of bonds to Re provided by the ligands of Re being equal to the coordination of Re

are disclosed.

Qualitative and quantitative electrochemiluminescent assays for analytes of interest present in multicomponent liquids using these moieties are disclosed. These methods comprise contacting a sample with a reagent labeled with an electrochemiluminescent chemical moiety containing rhenium and capable of combining with the analyte of interest, exposing the resulting sample to chemical, electrochemical, or electromagnetic energy and detecting electromagnetic radiation emitted by the electrochemiluminescent chemical moiety.
131 Claims, 3 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 3

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Image

☐ 12. Document ID: US 5807688 A

Entry 12 of 53 File: USPT Sep 15, 1998

US-PAT-NO: 5807688
DOCUMENT-IDENTIFIER: US 5807688 A

TITLE: Catalytic antibodies for carbamate activation by a non-spontaneous reaction mechanism

DATE-ISSUED: September 15, 1998

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Blackburn; George Michael	Sheffield	N/A	N/A	GBX
Wentworth; Paul	San Diego	CA	N/A	N/A

US-CL-CURRENT: 435/7.6; 424/175.1, 424/94.1, 435/188.5

ABSTRACT:

Catalytic antibodies capable of catalysing activation of a carbamate (--O--CO--NH--) containing prodrug suitable for Antibody Directed Abzyme Prodrug Therapy (ADAPT) by catalysing breakdown of the prodrug at the carbamate position by a non-spontaneous reaction mechanism. The non-spontaneous reaction preferably has a B.sub.Ac 2 mechanism and the prodrug is a preferably a nitrogen mustard aryl carbamate. The invention also includes relevant immunogens, screens for catalytic activity using short transition state analogues and ADAPT systems.
23 Claims, 117 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 108

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Image

☐ 13. Document ID: US 5804400 A

Entry 13 of 53 File: USPT Sep 8, 1998

US-PAT-NO: 5804400
DOCUMENT-IDENTIFIER: US 5804400 A

TITLE: Electrochemiluminescent assay

DATE-ISSUED: September 8, 1998

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Martin; Mark	North Bethesda	MD	N/A	N/A
Dong; Liwen	Rockville	MD	N/A	N/A

US-CL-CURRENT: 435/18; 205/255, 205/257, 205/264, 420/461, 420/462, 435/19, 435/23, 435/817, 435/968, 435/975

ABSTRACT:

A rapid single step assay suitable for the detection or quantification of enzymes, in particular, hydrolases, especially, aminopeptidases and esterases. The enzymatic reaction causes the cleavage of a metal ligand labelled hydrolase substrate. The cleaved ligand alters the electrochemiluminescence of bidentate aromatic heterocyclic nitrogen-containing ligand reagent. The change in electrochemiluminescence correlates to the presence of hydrolase activity present in the sample. The assay can be performed on an IGEN Origen.RTM. Analyzer.
48 Claims, 7 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 7

☐ 14. Document ID: US 5798083 A

Entry 14 of 53 File: USPT Aug 25, 1998

US-PAT-NO: 5798083
DOCUMENT-IDENTIFIER: US 5798083 A

TITLE: Apparatus for improved luminescence assays using particle concentration and chemiluminescence detection

DATE-ISSUED: August 25, 1998

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Massey; Richard J.	Rockville	MD	N/A	N/A
Blackburn; Gary F.	Gaithersburg	MD	N/A	N/A
Wilkins; Elizabeth W.	Germantown	MD	N/A	N/A
Shah; Haresh P.	Gaithersburg	MD	N/A	N/A

US-CL-CURRENT: 422/52; 436/172, 73/864

ABSTRACT:

What is described are methods and apparatus for performing a binding assay for an analyte of interest present in a sample. The methods include the steps of: forming a composition containing the sample, an assay-performance-substance which contains a component linked to a label compound capable of chemiluminescing when triggered, and a plurality of particles capable of specifically binding with the analyte and/or the assay-performance-substance; incubating the composition to form a complex which includes a particle and the labeled component; collecting the complex in a collection zone; introducing into the collection zone a trigger capable of triggering the label such that the label luminesces; and measuring the emitted luminescence to measure the presence of the analyte of interest in the sample.
22 Claims, 8 Drawing figures
Exemplary Claim Number: 21
Number of Drawing Sheets: 7

☐ 15. Document ID: US 5786141 A

Entry 15 of 53 File: USPT Jul 28, 1998

US-PAT-NO: 5786141
DOCUMENT-IDENTIFIER: US 5786141 A

TITLE: Electrogenerated chemiluminescence labels for analysis and/or referencing

DATE-ISSUED: July 28, 1998

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Bard; Allen J.	Austin	TX	78731	N/A
Richards; Thomas	Austin	TX	78746	N/A
Leland; Jonathan K.	Silver Spring	MD	20906	N/A

US-CL-CURRENT: 435/6; 435/5, 435/7.1, 435/91.1, 435/91.2, 436/149, 436/518, 530/300, 530/388.1, 536/26.6

ABSTRACT:

Biomolecule analysis using anodic oxidation of aqueous sodium 9, 10-diphenylanthracene-2-sulfonate (DPAS) and 1- and 2-thianthrenecarboxylic acid (1-THCOOH and 2-THCOOH) in the presence of tri-n-propylamine (TPrA) as a coreactant in aqueous solution produces electrogenerated chemiluminescence (ECL). In addition, the cathodic reduction of DPAS in the presence of peroxydisulfate (S.sub.2 O.sub.8.sup.2-) as a coreactant also produces ECL in an acetonitrile (MeCN)-water solution (1:1 by volume). The oxidation of chlorpromazine (CPZ) produces an ECL emission in the absence of an added coreactant following an unprecedented "self-annihilation" mechanism.
21 Claims, 32 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 20

☐ 16. Document ID: US 5779976 A

Entry 16 of 53 File: USPT Jul 14, 1998

US-PAT-NO: 5779976
DOCUMENT-IDENTIFIER: US 5779976 A

TITLE: Apparatus for improved luminescence assays

DATE-ISSUED: July 14, 1998

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Leland; Jonathan K.	Laurel	MD	N/A	N/A
Shah; Haresh P.	Pleasant Hill	CA	N/A	N/A
Kenten; John Henry	Gaithersburg	MD	N/A	N/A
Goodman; Jack E.	Arlington	VA	N/A	N/A
Lowke; George E.	Laytonsville	MD	N/A	N/A
Namba; Yuzaburo	Tsukuba	N/A	N/A	JPX
Blackburn; Gary F.	Gaithersburg	MD	N/A	N/A
Massey; Richard J.	Rockville	MD	N/A	N/A

US-CL-CURRENT: 422/52; 422/82.05, 436/172

ABSTRACT:

An apparatus for performing a binding assay for an analyte of interest present in a sample based upon measurement of electrochemiluminescence at an electrode surface comprising a cell defining a sample containing volume intersecting with inlet and outlet means, an electrode having a substantially horizontally positioned surface exposed to and positioned below a portion of the sample containing volume, means for impressing electrochemical energy upon said electrode sufficient to generate luminescence, means for magnetically collecting particles along said surface and means for measuring the luminescence generated at said electrode.
10 Claims, 25 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 21

☐ 17. Document ID: US 5770459 A

Entry 17 of 53 File: USPT Jun 23, 1998

US-PAT-NO: 5770459
DOCUMENT-IDENTIFIER: US 5770459 A

TITLE: Methods and apparatus for improved luminescence assays using particle concentration, electrochemical generation of chemiluminescence detection

DATE-ISSUED: June 23, 1998

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Massey; Richard J.	Rockville	MD	N/A	N/A
Blackburn; Gary F.	Gaithersburg	MD	N/A	N/A
Wilkins; Elizabeth W.	Germantown	MD	N/A	N/A
Leland; Jonathan K.	Laurel	MD	N/A	N/A

US-CL-CURRENT: 436/526; 435/7.1, 436/518, 436/524, 436/527, 436/528, 436/531, 436/532 , 436/533, 436/534, 436/537

ABSTRACT:

What is described are methods and apparatus for performing a binding assay for an analyte of interest present in a sample. The methods include the steps of: forming a composition containing said sample, an assay-performance-substance which contains a component linked to a label compound capable of chemiluminescing when triggered, and a plurality of coated magnetic particles capable of specifically binding with the analyte and/or said assay-performance-substance; incubating said composition to form a complex which includes a particle and said labeled component; magnetically collecting said complex at the surface of an electrode; inducing said label to luminesce by contacting it with a trigger, said trigger being formed in-situ by conversion of a precursor molecule upon introduction of electrochemical energy; and measuring the emitted luminescence to measure the presence of the analyte of interest in the sample.
23 Claims, 10 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 7

☐ 18. Document ID: US 5746974 A

Entry 18 of 53 File: USPT May 5, 1998

US-PAT-NO: 5746974
DOCUMENT-IDENTIFIER: US 5746974 A

TITLE: Apparatus for improved luminescence assays using particle concentration, electrochemical generation of chemiluminescence and chemiluminescence detection

DATE-ISSUED: May 5, 1998

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Massey; Richard J.	Rockville	MD	N/A	N/A
Blackburn; Gary F.	Gaithersburg	MD	N/A	N/A
Wilkins; Elizabeth W.	Germantown	MD	N/A	N/A
Leland; Jonathan K.	Laurel	MD	N/A	N/A

US-CL-CURRENT: 422/52; 422/82.05, 436/172

ABSTRACT:

What is described are methods and apparatus for performing a binding assay for an analyte of interest present in a sample. The methods include the steps of: forming a composition containing said sample, an assay-performance-substance which contains a component linked to a label compound capable of chemiluminescing when triggered, and a plurality of coated magnetic particles capable of specifically binding with the analyte and/or said assay-performance-substance; incubating said composition to form a complex which includes a particle and said labeled component; magnetically collecting said complex at the surface of an electrode; inducing said label to luminesce by contacting it with a trigger, said trigger being formed in-situ by conversion of a precursor molecule upon introduction of electrochemical energy; and measuring the emitted luminescence to measure the presence of the analyte of interest in the sample.
20 Claims, 10 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 7

☐ 19. Document ID: US 5731147 A

Entry 19 of 53 File: USPT Mar 24, 1998

US-PAT-NO: 5731147
DOCUMENT-IDENTIFIER: US 5731147 A

TITLE: Luminescent metal chelate labels and means for detection

DATE-ISSUED: March 24, 1998

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Bard; Allen J.	Austin	TX	N/A	N/A
Whitesides; George M.	Newton	MA	N/A	N/A

US-CL-CURRENT: 435/6; 435/7.1, 436/149, 436/150, 436/164, 436/172, 436/501, 436/536, 436/537, 436/805, 436/806, 436/82

ABSTRACT:

A chemical moiety is disclosed which comprises a chemical, biochemicals, or biological substance attached to one or more electrochemiluminescent organometallic compounds. In a preferred embodiment of the invention the substance is attached to one or more ruthenium-containing or osmium-containing luminescent organo-metallic compounds. Methods are disclosed for detecting low concentrations of the chemical moiety using chemiluminescent, electrochemiluminescent, and photo-luminescent means. Compounds are disclosed which are useful for labeling substances of interest with ruthenium-containing and osmium-containing labels or other electrochemiluminescent labels. These labeled substances are useful in methods provided for detecting and quantifying analytes of interest in binding assays and competitive binding assays. The labeled substances are of particular use in homogeneous binding assays. These methods form the bases for systems designed to enable the rapid, efficient, and sensitive determination of a broad array of chemical, biochemical, and biological materials of interest.
33 Claims, 0 Drawing figures
Exemplary Claim Number: 1

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Image

☐ 20. Document ID: US 5716781 A

Entry 20 of 53 File: USPT Feb 10, 1998

US-PAT-NO: 5716781
DOCUMENT-IDENTIFIER: US 5716781 A

TITLE: Method of calibration of an electrochemiluminescent assay system

DATE-ISSUED: February 10, 1998

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Massey; Richard J.	Rockville	MD	N/A	N/A
Powell; Michael J.	Gaithersburg	MD	N/A	N/A
Dressick; Walter J.	Gaithersburg	MD	N/A	N/A
Leland; Jonathan K.	Gaithersburg	MD	N/A	N/A
Hino; Janel K.	Arlington	VA	N/A	N/A
Poonian; Mohindar S.	Gaithersburg	MD	N/A	N/A
Ciana; Leopoldo Della	Gaithersburg	MD	N/A	N/A

US-CL-CURRENT: 435/6; 435/4, 435/5, 435/7.1, 435/7.2, 435/810, 436/501, 436/63, 536/24.3, 536/24.31, 536/24.32, 536/26.6

ABSTRACT:

Electrochemiluminiscent moieties having the formula

[Re(P).sub.m (L.sup.1).sub.n (L.sup.2).sub.o (L.sup.3).sub.p (L.sup.4).sub.q (L.sup.5).sub.r (L.sup.6).sub.s].sub.t (B).sub.u

wherein

P is a polydentate ligand of Re;

L.sup.1, L.sup.2, L.sup.3, L.sup.4, L.sup.5 and L.sup.6 are ligands of Re, each of which may be the same as or different from each other ligand;

B is a substance which is a ligand of Re or is conjugated to one or more of P, L.sup.1, L.sup.2, L.sup.3, L.sup.4, L.sup.5 or L.sup.6 ;

m is an integer equal to or greater than 1;

each of n, o, p, q, r and s is zero or an integer;

t is an integer equal to or greater than 1; and

u is an integer equal to or greater than 1;

P, L.sup.1, L.sup.2, L.sup.3, L.sup.4, L.sup.5, L.sup.6 and B being of such composition and number that the chemical moiety can be induced to emit electromagnetic radiation and the total number of bonds to Re provided by the ligands of Re being equal to the coordination of Re

are disclosed.

Qualitative and quantitative electrochemiluminescent assays for analytes of interest present in multicomponent liquids using these moieties are disclosed. These methods comprise contacting a sample with a reagent labeled with an electrochemiluminescent chemical moiety containing rhenium and capable of combining with the analyte of interest, exposing the resulting sample to chemical, electrochemical, or electromagnetic energy and detecting electromagnetic radiation emitted by the electrochemiluminescent chemical moiety.
12 Claims, 3 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 3

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Image

☐ 21. Document ID: US 5714089 A

Entry 21 of 53 File: USPT Feb 3, 1998

US-PAT-NO: 5714089
DOCUMENT-IDENTIFIER: US 5714089 A

TITLE: Luminescent metal chelatte labels and means for detection

DATE-ISSUED: February 3, 1998

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Bard; Allen J.	Austin	TX	N/A	N/A
Whitesides; George M.	Newton	MA	N/A	N/A

US-CL-CURRENT: 252/301.18; 252/301.16, 252/301.34, 252/301.35, 436/536, 436/800, 436/806, 546/2, 546/8

ABSTRACT:

A chemical moiety is disclosed which comprises a chemical, biochemical, or biological substance attached to one or more electrochemiluminescent organometallic compounds. In a preferred embodiment of the invention the substance is attached to one or more ruthenium-containing or osmium-containing luminescent organometallic compounds. Methods are disclosed for detecting low concentrations of the chemical moiety using chemiluminescent, electrochemiluminescent, and photoluminescent means. Compounds are disclosed which are useful for labeling substances of interest with ruthenium-containing and osmium-containing labels or other electrochemiluminescent labels. These labeled substances are useful in methods provided for detecting and quantifying analytes of interest in binding assays and competitive binding assays. The labeled substances are of particular use in homogeneous binding assays. These methods form the bases for systems designed to enable the rapid, efficient, and sensitive determination of a broad array of chemical, biochemical, and biological materials of interest.
13 Claims, 0 Drawing figures
Exemplary Claim Number: 1

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Image

☐ 22. Document ID: US 5705402 A

Entry 22 of 53 File: USPT Jan 6, 1998

US-PAT-NO: 5705402
DOCUMENT-IDENTIFIER: US 5705402 A

TITLE: Method and apparatus for magnetic microparticulate based luminescence assay including plurality of magnets

DATE-ISSUED: January 6, 1998

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Leland; Jonathan K.	Laurel	MD	N/A	N/A
Shah; Haresh P.	Gaithersburg	MD	N/A	N/A
Kenten; John H.	Gaithersburg	MD	N/A	N/A
Goodman; Jack E.	Arlington	VA	N/A	N/A
Lowke; George E.	Laytonsville	MD	N/A	N/A
Namba; Yuzaburo	Ibaraki	N/A	N/A	JPX
Blackburn; Gary F.	Gaithersburg	MD	N/A	N/A
Massey; Richard J.	Rockville	MD	N/A	N/A

US-CL-CURRENT: 436/526; 436/518, 436/524, 436/536, 436/537

ABSTRACT:

Disclosed and claimed are methods and apparatus for performing a binding assay for an analyte of interest present in a sample based upon measurement of electrochemiluminescence at an electrode. The method uses magnetically responsive particles. The method and apparatus call for a plurality of electromagnets or permanent magnets in north-south orientation for imposing a magnetic field so as to collect the particles.
8 Claims, 9 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 5

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Image

☐ 23. Document ID: US 5686244 A

Entry 23 of 53 File: USPT Nov 11, 1997

US-PAT-NO: 5686244
DOCUMENT-IDENTIFIER: US 5686244 A

TITLE: Method for detecting a nucleic acid analyte using an improved electrochemiluminescent label

DATE-ISSUED: November 11, 1997

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Gudibande; Satyanarayana R.	Rockville	MA	N/A	N/A
Kenten; John H.	Gaithersburg	MD	N/A	N/A

US-CL-CURRENT: 435/6; 252/700, 435/91.1, 435/91.2, 436/544, 436/546, 436/801, 436/94 , 536/23.1, 536/24.3

ABSTRACT:

This invention relates to a new electrochemiluminescent (ECL) label for oligonucleotides using phosphoramidite chemistry.
5 Claims, 0 Drawing figures
Exemplary Claim Number: 1

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Image

☐ 24. Document ID: US 5679519 A

Entry 24 of 53 File: USPT Oct 21, 1997

US-PAT-NO: 5679519
DOCUMENT-IDENTIFIER: US 5679519 A

TITLE: Multi-label complex for enhanced sensitivity in electrochemiluminescence assay

DATE-ISSUED: October 21, 1997

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Oprandy; John J.	Poolesville	MD	20837	N/A

US-CL-CURRENT: 435/6; 252/515, 435/5, 435/7.1, 435/7.9, 435/91.2, 536/24.3, 536/24.32 , 536/24.33, 536/26.6

ABSTRACT:

A nucleotide probe complex which enhances the ability to discriminate low level samples in electrochemiluminescent assays. The complex is composed of a platform molecule to which multiple copies of an organometallic electrochemiluminescent label and an oligonucleotide probe are separately attached. Preferably the complex is capped with streptavidin. Use of the complex permits detection of 1000 copies of analyte per sample in less than one hour.
20 Claims, 13 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 13

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Image

☐ 25. Document ID: US 5658753 A

Entry 25 of 53 File: USPT Aug 19, 1997

US-PAT-NO: 5658753
DOCUMENT-IDENTIFIER: US 5658753 A

TITLE: Catalytic antibody components

DATE-ISSUED: August 19, 1997

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Paul; Sudhir	Omaha	NE	68137	N/A
Powell; Michael J.	Danville	CA	94526	N/A
Massey; Richard J.	Rockville	MD	20852	N/A
Kenten; John H.	Gaithersburg	MD	20879	N/A

US-CL-CURRENT: 435/68.1; 435/188.5, 435/219, 435/226, 530/388.24, 530/389.2

ABSTRACT:

Catalytic antibody components, methods for producing catalytic antibody components, methods for using catalytic antibody components, in particular, single chain and smaller components are disclosed. Catalytic antibody components able to promote the cleavage or formation of an amide, peptide, ester or glycosidic bond, and which are prepared from monoclonal catalytic antibodies, catalytic autoantibodies or by site-directed mutagenesis are disclosed. Methods of using catalytic antibody components alone or in combination with other antibody components or other biological moieties are disclosed.
34 Claims, 19 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 15

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Image

☐ 26. Document ID: US 5658752 A

Entry 26 of 53 File: USPT Aug 19, 1997

US-PAT-NO: 5658752
DOCUMENT-IDENTIFIER: US 5658752 A

TITLE: Method of catalyzing chemical reactions

DATE-ISSUED: August 19, 1997

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Schochetman; Gerald	Rockville	MD	N/A	N/A
Massey; Richard J.	Rockville	MD	N/A	N/A

US-CL-CURRENT: 435/41; 435/188.5

ABSTRACT:

A method for increasing the rate of chemical reactions involving the conversion of at least one reactant to at least one product involves contacting the reactant with an appropriate monoclonal antibody under conditions permitting the formation of a complex between the antibody and the reactant. The complexed reactant is converted to the product which is then released from the complex. The monoclonal antibody may employ a cofactor and may be directed to a known substrate of an enzyme. Methods for preparing such monoclonal antibodies are also disclosed.
6 Claims, 0 Drawing figures
Exemplary Claim Number: 1

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Image

27. Document ID: US 5643713 A

Entry 27 of 53 File: USPT Jul 1, 1997

US-PAT-NO: 5643713
DOCUMENT-IDENTIFIER: US 5643713 A

TITLE: Electrochemiluminescent monitoring of compounds

DATE-ISSUED: July 1, 1997

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Liang; Pam	Arlington	VA	22209	N/A
Martin; Mark T.	N. Bethesda	MD	20852	N/A
Dong; Liwen	Rockville	MD	20850	N/A

US-CL-CURRENT: 435/4; 435/18, 435/29, 435/34, 435/39, 435/7.1, 435/7.2, 435/7.32, 435/7.72, 436/4, 549/34

ABSTRACT:

Detectable compounds comprising a chemically-transformable first compound covalently linked to an electrochemiluminescent compound are provided. Such compounds are useful in processes and kits that monitor the status of the first compound and derive information from such monitoring.
20 Claims, 19 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 17

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Image

28. Document ID: US 5641865 A

Entry 28 of 53 File: USPT Jun 24, 1997

US-PAT-NO: 5641865
DOCUMENT-IDENTIFIER: US 5641865 A

TITLE: Interaction system comprising a surfactant-stabilized disperse aqueous phase containing an antibody or antibody fragment

DATE-ISSUED: June 24, 1997

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Durfor; Charles N.	Rockville	MD	N/A	N/A
Bolin; Richard J.	Fairfax	VA	N/A	N/A
Schantz, II; Allen R.	Reston	VA	N/A	N/A
Massey; Richard J.	Rockville	MD	N/A	N/A

US-CL-CURRENT: 435/7.1; 428/402.2, 435/188.5, 436/535, 436/548, 436/829, 516/25, 530/387.1, 530/388.1, 530/812

ABSTRACT:

An interaction system, including an antibody or, antibody fragment having functional capability, which comprises a surfactant-stabilized microheterogeneous dispersion of aqueous phase in a water-immiscible medium, said aqueous phase containing an amount of said antibody or said fragment in a functional state sufficient to effect the interaction; and methods for making and for using said system.
22 Claims, 6 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 5

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Image

☐ 29. Document ID: US 5641623 A

Entry 29 of 53 File: USPT Jun 24, 1997

US-PAT-NO: 5641623
DOCUMENT-IDENTIFIER: US 5641623 A

TITLE: Electrochemiluminescence assay

DATE-ISSUED: June 24, 1997

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Martin; Mark T.	N. Bethesda	MD	20852	N/A

US-CL-CURRENT: 435/4; 424/1.69, 435/18, 435/29, 435/34, 435/39, 435/7.1, 435/7.2, 435/7.32, 435/7.72, 549/34

ABSTRACT:

A rapid single step assay suitable for the detection or quantification of .beta.-lactam antibiotics and .beta.-lactamases. The assay can be performed directly on samples of food, such as milk and meat, blood or serum and is useful in determining the suitability of a particular antibiotic in treating a particular bacterial infection and in diagnosis of a bacterial infection. The assay is also useful in determining and quantifying .beta.-lactam antibiotic resistance. The assay can be performed on an IGEN Origen.sup.R Analyzer.
31 Claims, 10 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 7

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Image

☐ 30. Document ID: US 5635347 A

Entry 30 of 53 File: USPT Jun 3, 1997

US-PAT-NO: 5635347
DOCUMENT-IDENTIFIER: US 5635347 A

TITLE: Rapid assays for amplification products

DATE-ISSUED: June 3, 1997

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Link; John R.	Springfield	VA	N/A	N/A
Gudibande; Satyanarayana R.	Rockville	MD	N/A	N/A
Kenten; John H.	Gaithersburg	MD	N/A	N/A

US-CL-CURRENT: 435/6; 435/91.2, 435/91.5, 436/164, 436/172, 536/24.3

ABSTRACT:

A method of detecting a nucleic acid sequence of interest in the amplification product of a polymerase chain reaction or other primer directed reaction comprising the steps of:

(a) incorporating in a polymerase chain reaction mixture or other primer directed reaction mixture at least one nucleic acid sequence complementary to said nucleic acid sequence of interest labeled (i) at the 3' end thereof, or (ii) at the 3' and the 5' end thereof with a compound capable of electrochemiluminescence;

(b) conducting a polymerase chain reaction or other primer directed reaction; and

(c) measuring the electrochemiluminescence of labeled amplification product.
7 Claims, 6 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 3

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Image

☐ 31. Document ID: US 5610017 A

Entry 31 of 53 File: USPT Mar 11, 1997

US-PAT-NO: 5610017
DOCUMENT-IDENTIFIER: US 5610017 A

TITLE: Method for conducting a polymerase chain reaction using an improved electrochemiluminescent label

DATE-ISSUED: March 11, 1997

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Gudibande; Satyanarayana R.	Rockville	MA	N/A	N/A
Kenten; John H.	Gaithersburg	MD	N/A	N/A

US-CL-CURRENT: 435/6; 428/917, 435/183, 435/91.1, 435/91.2, 436/800, 436/805, 436/905 , 436/94, 536/23.1, 536/24.32, 536/24.33, 536/25.3

ABSTRACT:

This invention relates to a new electrochemiluminescent (ECL) label for oligonucleotides using phosphoramidite chemistry.
1 Claims, 0 Drawing figures
Exemplary Claim Number: 1

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Image

☐ 32. Document ID: US 5602015 A

Entry 32 of 53 File: USPT Feb 11, 1997

US-PAT-NO: 5602015
DOCUMENT-IDENTIFIER: US 5602015 A

TITLE: Autoantibodies which enhance the rate of a chemical reaction

DATE-ISSUED: February 11, 1997

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Sudhir; Paul	Omaha	NE	N/A	N/A

US-CL-CURRENT: 435/188.5; 435/219, 435/226

ABSTRACT:

Autoantibodies which enhance the rate of a chemical reaction of a substrate, processes for their preparation, their use and compositions thereof are disclosed. In particular, an autoantibody capable of catalyzing the hydrolysis of the peptide bond between amino acid residues Thr.sup.7 -Asp.sup.8, Arg.sup.14 -Lys.sup.15, Gln.sup.16 -Met.sup.17, Met.sup.17 -Ala.sup.18, Ala.sup.18 -Val.sup.19, Lys.sub.20 -Lys.sup.21, Lys.sup.21 -Tyr.sup.22 in the neurotransmitter vasoactive intestinal peptide (VIP) is disclosed.
46 Claims, 24 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 20

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Image

☐ 33. Document ID: US 5599538 A

Entry 33 of 53 File: USPT Feb 4, 1997

US-PAT-NO: 5599538
DOCUMENT-IDENTIFIER: US 5599538 A

TITLE: Autoantibodies which enhance the rate of a chemical reaction

DATE-ISSUED: February 4, 1997

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Paul; Sudhir	Omaha	NE	N/A	N/A
Li; Lan	Omaha	NE	N/A	N/A
Kaveri; Srini	Villejuif	N/A	N/A	FRX

US-CL-CURRENT: 424/130.1; 424/143.1, 424/175.1, 424/94.1, 435/188.5

ABSTRACT:

Autoantibodies which enhance the rate of a chemical reaction of a substrate, processes for their preparation, their use and compositions thereof are disclosed. In particular, an autoantibody capable of catalyzing the hydrolysis of the peptide bond between amino acid residues 16 and 17 in the neurotransmitter vasoactive intestinal peptide (VIP) is disclosed. Human anti-thyroglobulin antibodies isolated by chromatography on protein-A and immobilized Tg hydrolyzed radiolabeled Tg, as shown by generation of several lower-sized products on SDS-electrophoresis gels. The activity displayed a K.sub.m value of a 39 nM property typical of an antibody-combining site. Tg-antibodies also hydrolyzed commercially available peptidyl-methylcoumarinamide (MCA) substrates, displaying a preference for arg-MCA and lys-MCA containing conjugates. The hydrolysis of pro-phe-arg-MCA was characterized by K.sub.m (17 .mu.M) and k.sub.cat 0.06 min.sup.-1. Peptidyl-MCA hydrolysis was inhibited potently by thyroglobulin (K.sub.i 24 nM), suggesting a catalytic site/located in the antibody combining site. In control experiments, the hydrolytic activities were removed by immunoadsorption with immobilized anti-human IgG, and IgG depleted of the Tg-specific antibodies by affinity chromatography did not display Tg and pro-phe-arg-MCA hydrolyzing activities.
8 Claims, 27 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 22

☐ 34. Document ID: US 5597910 A

Entry 34 of 53 File: USPT Jan 28, 1997

US-PAT-NO: 5597910
DOCUMENT-IDENTIFIER: US 5597910 A

TITLE: Electrochemiluminescent label for DNA probe assays

DATE-ISSUED: January 28, 1997

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Gudibande; Satyanarayana R.	Rockville	MA	N/A	N/A
Kenten; John H.	Gaithersburg	MD	N/A	N/A

US-CL-CURRENT: 536/24.3; 250/361C, 252/301.16, 435/6, 435/91.1, 436/800, 436/801, 536/25.3, 536/25.32

ABSTRACT:

This invention relates to a new electrochemiluminescent (ECL) label for oligonucleotides using phosphoramidite chemistry.
9 Claims, 0 Drawing figures
Exemplary Claim Number: 1

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Image

☐ 35. Document ID: US 5597573 A

Entry 35 of 53 File: USPT Jan 28, 1997

US-PAT-NO: 5597573
DOCUMENT-IDENTIFIER: US 5597573 A

TITLE: Lipid-A analogs: new monosaccharide and disaccharide intermediates for eliciting therapeutic antibodies and for antitumor and antiviral activities

DATE-ISSUED: January 28, 1997

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Kamireddy; Balreddy	Hockessin	DE	N/A	N/A
Darsley; Michael J.	Rockville	MD	N/A	N/A
Simpson; David M.	Adelphi	MD	N/A	N/A
Massey; Richard J.	Rockville	MD	N/A	N/A

US-CL-CURRENT: 424/234.1; 424/283.1, 514/25, 536/17.1, 536/17.3, 536/17.4, 536/18.7

ABSTRACT:

The present invention relates to novel amidine components of formula (II): ##STR1## A method for eliciting antibodies in an animal which bind to Lipid A or LPS comprising administering to the animal as an immunogen a composition comprising such a compound is also disclosed.
6 Claims, 53 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 53

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Image

☐ 36. Document ID: US 5593969 A

Entry 36 of 53 File: USPT Jan 14, 1997

US-PAT-NO: 5593969
DOCUMENT-IDENTIFIER: US 5593969 A

TITLE: Lipid-A analogs: monosaccharide and dissaccharide compounds for inhibiting binding of lipid A receptors to lipid A receptors

DATE-ISSUED: January 14, 1997

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Kamireddy; Balreddy	Rockville	MD	N/A	N/A
Darsley; Michael J.	Rockville	MD	N/A	N/A
Simpson; David M.	Adelphi	MD	N/A	N/A
Massey; Richard J.	Rockville	MD	N/A	N/A

US-CL-CURRENT: 514/25; 514/53, 514/54, 536/117, 536/17.1, 536/18.7, 536/52, 536/53, 536/55.3

ABSTRACT:

A compound of the formula: ##STR1## wherein: each of R.sub.1, R.sub.1 ', R.sub.2 and R.sub.2 ' independent of each other is a substituted or unsubstituted, branched or linear C.sub.1-12 alkyl, alkene or alkyne group, R.sub.3 is OH, OCH.sub.3, CH.sub.2 COOH or ##STR2## wherein each of R.sub.2" and R.sub.2 '41 independent of each other is a substituted or unsubstituted, branched or linear C.sub.1-12 alkyl, alkene or alkyne group and:

A=NH.sub.2, X=P(OH), Y=Z=C, B=OCH.sub.3, or

A=OH, X=P(OH), X=Z=C, B (if present)=OCH.sub.3, or

A=OCO(CH.sub.2).sub.n NH.sub.2, X=P(OH), Y=Z=C, B=OCH.sub.3,

wherein n=1-10, or

A=OH, X=P(OH), Y=Z=C, B=O(CH.sub.2).sub.n CO.sub.2 H, wherein n=1-10, or

A=OH, X=P(OH), Y=Z=C, B=(CH.sub.2).sub.n CO.sub.2 H, wherein n=1-10, or

A=NH.sub.2, X=Z=C, Y=P(OH), B=OCH.sub.3, or

A=OH, X=Z=C, Y=P(OH), B (if present)=OCH.sub.3, or

A=OCO(CH.sub.2).sub.n NH.sub.2, X=Z=C, Y=P(OH), B=OCH.sub.3, wherein n=1-10, or

A=OH, X=Z=C, Y=P(OH), B=O(CH.sub.2).sub.n CO.sub.2 H, wherein n=1-10, or

A=OH, X=Z=C, Y=P(OH), B=(CH.sub.2).sub.n CO.sub.2 H, wherein n=1-11, or

A=NH.sub.2, X=Y=C, Z=P(OH),. B=OCH.sub.3, or

A=OH, X=Y=C, Z=P(OH), B (if present)=OCH.sub.3, or

A=OCO(CH.sub.2).sub.n NH.sub.2, X=Y=C, Z=P(OH), B=OCH.sub.3, wherein n=1-10, or

A=OH, X=Y=C, Z=P(OH), B=O(CH.sub.2).sub.n CO.sub.2 H, wherein n=1-10, or

A=OH, X=Y=C, Z=P (OH), B=(CH.sub.2).sub.n CO.sub.2 H and n=1-11 is disclosed. The compounds may be use to inhibit binding of Lipid A to Lipid A receptors.
4 Claims, 47 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 47

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Image

☐ 37. Document ID: US 5591581 A

Entry 37 of 53 File: USPT Jan 7, 1997

US-PAT-NO: 5591581
DOCUMENT-IDENTIFIER: US 5591581 A

TITLE: Electrochemiluminescent rhenium moieties and methods for their use

DATE-ISSUED: January 7, 1997

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Massey; Richard J.	Rockville	MD	N/A	N/A
Powell; Michael J.	Gaithersburg	MD	N/A	N/A
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Ciana; Leopoldo D.	Gaithersburg	MD	N/A	N/A

US-CL-CURRENT: 435/6; 435/235.1, 435/325, 435/410, 435/5, 435/7.2, 436/537, 530/350, 530/400, 546/2, 556/45, 556/46, 556/49

ABSTRACT:

Electrochemiluminescent moieties having the formula

(Re(P).sub.m (L.sup.1).sub.n (L.sup.2).sub.o (L.sup.3).sub.p (L.sup.4).sub.t (B).sub.u

wherein

P is a polydentate ligand of Re;

L.sup.1, L.sup.2, L.sup.3 and L.sup.4 are ligands of Re, each of which may be the same as or not the same as each other ligand;

B is a substance which is a ligand of Re or is conjugated to one or more of P, L.sup.1, L.sup.2, L.sup.3 and L.sup.4 ;

m is an integer equal to or greater than 1;

each of n, o, p, q, r and s is zero or an integer;

t is an integer equal to or greater than 1; and

u is an integer equal to or greater than 1;

P, L.sup.1, L.sup.2, L.sup.3, L.sup.4 and B being of such composition and number that the chemical moiety can be induced to electrochemiluminesce and the total number of bonds to Re provided by the ligands of Re being equal to the coordination number of Re are disclosed.

Qualitative and quantitative electrochemiluminescent assays for analytes of interest present in multicomponent liquids using these moieties are also disclosed.
20 Claims, 3 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 3

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Image

☐ 38. Document ID: US 5541113 A

Entry 38 of 53 File: USPT Jul 30, 1996

US-PAT-NO: 5541113
DOCUMENT-IDENTIFIER: US 5541113 A

TITLE: Method for detecting an analyte using an electrochemical luminescent transition metal label

DATE-ISSUED: July 30, 1996

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Siddigi; Iqbal W.	Brea	CA	N/A	N/A
Sternberg; James C.	Fullerton	CA	N/A	N/A

US-CL-CURRENT: 436/56; 422/52, 422/82.05, 422/82.06, 422/82.08, 436/164, 436/172

ABSTRACT:

A method for detecting an analyte, in an aqueous solution at a physiological pH, by reductive or oxidative/reductive electrochemical luminescence methodologies is disclosed. The method proceeds by labelling the analyte with a transition metal complex, followed by inducing the transition metal label to luminescence by application of a suitable electrical potential to a solution containing the label and the analyte. The transition metal complex can be a tris-ruthenium(bipyridine) complex. A hydroxylamine and/or a halogen-containing moiety can be used to enhance both reductive and/or oxidative electrochemical luminescence of the transition metal complex. The transition metal chelate can be used as a label for the detection of picomolar concentrations of an analyte of interest, such as an analyte present in a sample of a physiological fluid.
36 Claims, 14 Drawing figures
Exemplary Claim Number: 22
Number of Drawing Sheets: 11

☐ 39. Document ID: US 5527710 A

Entry 39 of 53 File: USPT Jun 18, 1996

US-PAT-NO: 5527710
DOCUMENT-IDENTIFIER: US 5527710 A

TITLE: Rate measurements of biomolecular reactions using electrochemiluminescence

DATE-ISSUED: June 18, 1996

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Nacamulli; Laurette	Rockville	MD	N/A	N/A
Leland; Jonathan K.	Silver Spring	MD	N/A	N/A
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US-CL-CURRENT: 436/517; 422/52, 422/82.01, 422/82.05, 422/82.08, 435/4, 435/6, 435/7.1, 435/7.5, 436/149, 436/172, 436/501, 436/536, 436/537, 436/544 , 436/546

ABSTRACT:

The rate of a biomolecular reaction, such as an enzymatic reaction or an affinity binding reaction, is measured using electrochemiluminescence ("ECL"). The reaction is conducted in an electrochemical cell with a mixture of reagents including a luminophore which will relate the concentration of a reactant, a reaction partner or the reaction product of a reaction partner to the ECL intensity. The reaction partner is a reagent which reacts with the reactant and which participates with the luminophore (or its reaction product participates with the luminophore) to cause the emission of ECL. The ECL intensity is modulated with a series of electrical pulses which are applied to the mixture of reagents at a preselected potential and for preselected intervals of time and duration. The ECL intensity is measured at the same intervals to provide a timed series of values (P). The same experiment is repeated except that the modulation is conducted after the reaction has gone to completion to obtain a timed series of values (C). The same experiment is repeated a third time in the absence of the reaction partner to obtain a times series of values (B). The results are normalized (N) using the following formula: ##EQU1## to obtain a series of values N which can be used to plot the time course (concentration vs. time) of the reaction.
36 Claims, 0 Drawing figures
Exemplary Claim Number: 1

☐ 40. Document ID: US 5453356 A

Entry 40 of 53 File: USPT Sep 26, 1995

US-PAT-NO: 5453356
DOCUMENT-IDENTIFIER: US 5453356 A

TITLE: Luminescent metal chelate labels and means for detection

DATE-ISSUED: September 26, 1995

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Bard; Allen J.	Austin	TX	N/A	N/A
Whitesides; George M.	Newton	MA	N/A	N/A

US-CL-CURRENT: 435/6; 435/7.1, 435/7.2, 435/7.31, 436/172, 436/500, 436/501, 436/517 , 436/518, 436/536, 436/544, 436/547, 436/548, 436/805, 436/806, 436/84

ABSTRACT:

A chemical moiety is disclosed which comprises a chemical, biochemical, or biological substance attached to one or more electrochemiluminescent organometallic compounds. In a preferred embodiment of the invention the substance is attached to one or more ruthenium-containing or osmium-containing luminescent organometallic compounds. Methods are disclosed for detecting very small amounts of the chemical moiety using chemiluminescent, electrochemiluminescent, and photoluminescent means. Compounds are disclosed which are useful for labelling substances of interest with ruthenium-containing and osmium-containing labels or other electrochemiluminescent labels. These labelled substances are useful in methods provided for detecting and quantifying analytes of interest in binding assays and competitive binding assays. The labelled substances are of particular use in homogeneous binding assays. These methods form the bases for systems designed to enable the rapid, efficient, and sensitive determination of a broad array of chemical, biochemical, and biological materials of interest.
75 Claims, 0 Drawing figures
Exemplary Claim Number: 1

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